NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 232

CARCINOGENESIS BIOASSAY OF PENTACHLOROETHANE

(CAS NO. 76-01-7)

IN F344/N RATS AND B6C3F$_1$ MICE (GAVAGE STUDY)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/ validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT
ON THE

CARCINOGENESIS BIOASSAY OF PENTACHLOROETHANE

(CAS NO. 76-01-7)

IN F344/N RATS AND B6C3F$_1$ MICE
(GAVAGE STUDY)

NATIONAL TOXICOLOGY PROGRAM
Box 12233
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Public Health Service
National Institutes of Health

NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical has the potential for hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in the report is encouraged to make this information known to the NTP.

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650).

Single copies of this carcinogenesis bioassay technical report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

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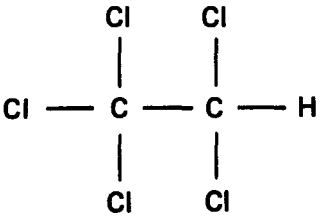

PENTACHLOROETHANE

CAS NO. 76-01-7
C_2HCl_5 Mol. Wt. 202.30

ABSTRACT

A carcinogenesis bioassay of technical grade pentachloroethane (95.5% pure, with 4.2% hexachloroethane) was conducted by administering the test chemical in corn oil by gavage to groups of 50 male and 50 female F344/N rats at doses of 75 or 150 mg/kg body weight and to groups of 50 male and 50 female $B6C3F_1$ mice at doses of 250 or 500 mg/kg. Doses were administered for 103 weeks for rats and 41-103 weeks for mice. Groups of 50 rats and 50 mice of each sex received corn oil by gavage on the same dosing schedule and served as vehicle controls. Prechronic testing (single-dose and 14-day and 13-week repeated-dose studies) did not indicate target organ toxicity for pentachloroethane. The dosage levels for the 2-year study were selected on the basis of survival and body weight gains during the prechronic test phase.

Survival of high-dose rats of each sex was significantly ($P < 0.05$) less than that of the controls. Mean body weights of dosed male and female rats were lower than those of the corresponding controls during the second year of the study. Final mean body weights for rats were 4%-5% lower for male rats and 8%-12% lower for female rats when compared to controls.

Chronic, diffuse inflammation of the kidney, distinguishable from nephropathy seen in aging F344/N rats, was found in male rats in a significant ($P < 0.001$) and dose-related incidence (control, 4/50, 8%; low-dose, 14/49, 29%; high-dose, 33/50, 66%). Mineralization of the renal papilla, considered to be secondary to chronic inflammation, was also observed at increased incidences in dosed male rats.

Pentachloroethane administration did not cause any increased incidences of tumors in either male or female rats. [See Note Added Subsequent to Peer Review on page 8.] Statistically significant negative trends were detected for subcutaneous tissue fibromas among males and for pituitary adenomas in both sexes.

Forty-two high-dose male mice died by week 41, and the 8 remaining animals in the group were killed at that time. Twenty-five male control mice were killed at week 44 to serve as controls for the high-dose males. Only 22/50 (44%) of the low-dose male mice survived to the end of the study. All high-dose female mice were dead by week 74, and only 9/50 (18%) low-dose females survived to the end of the study. Mean body weights of mice were lower than those of controls.

The incidence of hepatocellular carcinoma was significantly elevated in all groups of dosed mice (male: 4/48, 8%; 26/44, 59%, $P < 0.001$; 7/45, 16%; female: 1/46, 2%; 28/42, 67%, $P < 0.001$; 13/45, 29% $P < 0.001$). Early mortalities in the high-dose male mice precluded an evaluation of their lifetime incidence of hepatocellular carcinoma. There was a significant increase in incidence over that observed among 25 controls killed at week 44 (0/25 versus 7/45, $P<0.05$). There was also a significant ($P < 0.001$) dose-related increase in hepatocellular adenoma in female mice (2/46, 4%; 8/42, 19%; 19/45, 42%).

Under the conditions of this bioassay, technical grade pentachloroethane containing 4.2% hexachloroethane (a known carcinogen in mice) was not carcinogenic in F344/N rats. The decreased survival of dosed rats might have reduced the sensitivity for a carcinogenic response in this species. Pentachloroethane was nephrotoxic to male rats. Technical grade pentachloroethane was carcinogenic for $B6C3F_1$ mice, causing hepatocellular carcinomas in males and females, and adenomas in females.

NOTE ADDED SUBSEQUENT TO PEER REVIEW

After the Peer Review Panel meeting in June 1981, the National Toxicology Program determined that the kidney (especially in male F344/N rats) was a target organ for the short-chain chlorinated aliphatic hydrocarbons. This awareness came from the nonneoplastic and neoplastic diagnoses made on related chemicals in this class. Alerted to this lead, the NTP re-examined the originally-prepared histology slides on the rat kidney from the pentachloroethane bioassay. During the re-reading, additional renal tubular adenomas were discovered. Unfortunately, these slides were lost after they arrived at the Gulf South Research Institute laboratory; by necessity, a new set of slides was prepared.

In the second set of slides, three additional renal tubular-cell adenomas were discovered: one in a low-dose male and two in high-dose males; none were found in treated females or in male and female vehicle controls. Thus, rare tubular-cell adenomas of the kidney occurred in male rats with a dose-related trend ($P < 0.05$), and the incidence in the high-dose group was suggestive ($P < 0.06$; 0/50, 1/49, 4/50). Additionally, one control and one low-dose male each had an adenocarcinoma and another low-dose male had a carcinoma of the kidney (not otherwise specified); combining tubular-cell tumors reduced the statistical differences (1/50, 2/49, 4/50). These tumors are uncommon in male vehicle controls in the bioassay program, occurring in 1/293 (0.3%) at this bioassay testing laboratory and in 4/998 (0.4%) in all NCI/NTP bioassay testing laboratories. All tumors in these gavage controls were adenocarcinomas. The National Toxicology Program considers that these rare tubular-cell tumors of the kidney in male rats indicate a target organ and may have been associated with the administration of pentachloroethane. These additional tumor diagnoses were not presented to the Peer Review Panel. These are, however, the incidence rates recorded and analyzed statistically in this technical report (Table 5, Table A1, and Table A3).

CONTRIBUTORS

The bioassay of pentachloroethane was conducted at Gulf South Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The 2-year study was begun in December 1977 and completed in December 1979.

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The pathology report and selected slides were evaluated on 14 and 19 November 1980 by the NTP Pathology Working Group, which was composed of Drs. G. Boorman (NTP), B. Gupta (NTP), P. Hildebrandt (Tracor Jitco), G. Reznik (NTP), and J. Ward (NTP).

The chemicals used in this bioassay of pentachloroethane were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110. Reanalysis of the bulk chemical and analysis of chemical/vehicle mixtures were performed at Gulf South Research Institute.

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SUMMARY OF PEER REVIEW COMMENTS

On June 23, 1981, this carcinogenesis bioassay report on pentachloroethane underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts at an open meeting held in Building 101, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

Dr. Harper, as the principal reviewer for the report on the bioassay of pentachloroethane, agreed with the conclusion that, under the conditions of the bioassay, technical grade pentachloroethane, containing 4.2 percent hexachloroethane, was carcinogenic for $B6C3F_1$ mice of either sex, causing increased incidences of hepatocellular carcinoma. The carcinogenicity of the test material may have been influenced by the presence of hexachloroethane, a known liver carcinogen in mice. Technical grade pentachloroethane was nephrotoxic for male (but not female) F344/N rats, but was not carcinogenic for either sex. Dr. Harper added that decreased survival of dosed rats might have contributed to the absence of a carcinogenic effect in F344/N rats. As a general comment, he noted the bioassays of halogenated hydrocarbons continue to be plagued with problems of poor survival in rats. He said the report alluded to the fact that pentachloroethane is metabolized to trichloroethylene, which was positive for carcinogenicity in an earlier bioassay. In that study, trichloroethylene was contaminated with epichlorohydrin and 1,2-epoxybutane, both powerful alkylating agents. This might be noted in the discussion. Dr. J. Douglas, NTP, reported that pathology results from another trichloroethylene bioassay should be available to cite in this report in response to Dr. Harper's question.

As the second principal reviewer, Dr. Breslow commented on the interpretation of the early mortality, specifically the significant increase in incidence of hepatocellular carcinoma in high-dose mice that was found by comparing the proportions of affected animals among those dying or killed by 44 weeks: 7/45 vs 0/25 in controls, $P = 0.049$. Since the analysis accounts for the number of animals at risk, he felt it was misleading to claim that early mortality was primarily responsible for the effect. A suggested rewording in the abstract and discussion would be: Early mortality of high-dose mice precluded an evaluation of their life-time incidence of hepatocellular carcinoma. There was a significant increase in incidence over that observed among 25 controls killed at week 44. In addition to the nephropathy previously noted, he said there was a significant dose-related trend in the incidence of interstitial inflammation of the lung for male rats.

Dr. Mirer stated he could see no justification for the use of technical grade material contaminated with other toxic compounds, and this usage interferes with interpretation of the significance of the results. In the future, some thought should be given as to when it is appropriate to use technical rather than reagent grade material. Dr. Swenberg also objected to the wording both in the Appendix and in the section on results in mice that the early mortality was responsible for the slight increase in tumors. He said the lack of pathologic data for the subchronic study was a major omission. Dr. Moore said he thought it had been included, but in any event, there were no pathological findings.

Dr. Harper moved that the report on the bioassay of pentachloroethane be accepted. Dr. Breslow seconded the motion, with the suggested modifications, and the technical report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

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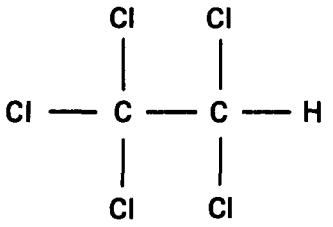

PENTACHLOROETHANE

CAS NO. 76-01-7
C_2HCl_5 Mol. Wt. 202.30

Pentachloroethane (pentalin) is a solvent that was used primarily as an intermediate in the manufacture of tetrachloroethylene (Kirk-Othmer, 1979). With the development of alternate manufacturing processes for tetrachloroethylene, the annual production of pentachloroethane has declined to less than 5,000 pounds (USITC, 1980).

Exposure to pentachloroethane vapor produces irritation of the eyes and respiratory tract and mild narcosis in humans (International Technical Information Institute, 1975). The lowest published lethal concentrations of pentachloroethane, administered by inhalation to rats and mice, are 4,238 ppm and 35 g/m^3, respectively (International Technical Information Institute, 1975). Single subcutaneous injections of pentachloroethane at doses of 1,100-1,800 mg/kg produced no deaths in female NMRI mice up to 72 hours after administration, and 12%-51% of the dose was expired unchanged (Yllner, 1971). The metabolites trichloroethanol (16%-32% of the dose) and trichloroacetic acid (9%-18% of the dose) were excreted in the urine, and trichloroethylene (2%-16% of the dose) and tetrachloroethylene (3%-9% of the dose) were identified in the expired air (Yllner, 1971).

Chlorinated ethanes and ethylenes are commercially important chemicals, several of which have been found to produce cancer in laboratory animals. For example, 1,2-dichloroethane, administered by gavage, increased the incidence of tumors in both sexes of B6C3F1 mice and Osborne-Mendel rats (NCI, 1978d). The more consistent pattern of response to chloroethanes and ethylenes has been an increase in hepatocellular carcinoma in B6C3F1 mice with little or no carcinogenicity apparent in Osborne-Mendel rats (NCI, 1976; 1977; 1978a; 1978b; 1978c). The results of these earlier carcinogenicity studies have been summarized (Weisburger, 1977) and reviewed (IARC, 1979).

The apparent absence of carcinogenic effects in Osborne-Mendel rats has been difficult to interpret because the treatment regimens employed generally shortened the survival times of the test animals. Therefore, the failure of the treatments to increase tumor incidences in the rats could have been due to the fact that the animals did not live long enough to develop the lesions. In most of the earlier studies, however, the survival times of both rats and mice were adversely affected by the treatments.

It is possible that the apparent lack of susceptibility of the Osborne-Mendel rat, or of rats in general, to the carcinogenic action of the chloroethanes and ethylenes is a genetic phenomenon. This possibility prompted the National Cancer Institute/National Toxicology Program to assess the carcinogenicity of several chlorohydrocarbons in different rat strains as well as in B6C3F1 mice. These studies were also initiated because some in this class of chemicals had been either inadequately studied or not studied at all. Pentachloroethane was in the latter category. While most of these studies are still in progress, the comparative testing of pentachloroethane in B6C3F1 mice and Fischer 344/N rats is completed. This report summarizes the results of that study.

Pentachloroethane did not induce any mutagenic response in *Salmonella typhimurium* strains TA 98, 100, 1535, and 1537 (with or without metabolic activation). Exogenous metabolic activation was provided by 9,000 x g liver supernatant (S-9) fractions from Aroclor 1254-induced male Sprague-Dawley rats and male Syrian hamsters (NTP, 1982; NTP unpublished results).

II. MATERIALS AND METHODS

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CHEMICAL ANALYSIS

The technical grade pentachloroethane used in this bioassay was obtained from Columbia Organic Chemicals (Columbia, SC) in two batches. Lot No. CO41676 (89.5% pure) was used for the subchronic studies, and Lot No. CO102077 (95.5% pure) was used for the chronic studies. Both lots were stored at -20°C.

Elemental analyses agreed with theoretical values, and infrared and nuclear magnetic resonance spectra agreed with literature values (Appendixes E and F).

The impurities identified and quantitated are listed in Table 1. The technical-grade pentachloroethane was considered to be representative of the commercially available compound, and it was therefore judged to be suitable for use in the carcinogenesis bioassay. Gulf South Research Institute also analyzed the chemical periodically throughout the study using infrared spectroscopy and gas chromatography. There was no significant difference between the results, indicating that chemical decomposition had not taken place.

TABLE 1. IMPURITIES IDENTIFIED IN PENTACHLOROETHANE

Chemical	Percent of Major Peak	
	Lot No. CO41676 *(a)*	Lot No. CO102077 *(b)*
Acetone	—	0.08 *(c)*
Hexachloroethane	10.40 *(d)*	4.20 *(c)*
Pentachlorobutadiene	—	*(e)*
1,2,4,4-Tetrachlorobutadiene	—	*(e)*
1,1,1,2-Tetrachloroethane	<0.01 *(d)*	—
1,1,2,2-Tetrachloroethane	<0.01 *(d)*	0.03 *(c)*
Tetrachloroethylene	0.55 *(d)*	0.05 *(c)*
Trichloroethylene	<0.01 *(d)*	0.13 *(c)*
1,1,1-Trichloropropane	—	<0.01 *(c)*

(a) Used in subchronic studies

(b) Used in chronic studies

(c) Quantitated by vapor-phase chromatography.

(d) Quantitated using vapor-phase chromatography/mass spectrometry.

(e) Identified by mass spectrometry but not quantitated.

ANIMALS

F344/N rats and B6C3F$_1$ mice of each sex were used throughout these studies. Animals used in the prechronic studies were obtained from the Frederick Cancer Research Center (Frederick, MD), and those used in the chronic studies were obtained from the Charles River Breeding Laboratories (Portage, MI). All animals were acclimated to laboratory conditions for 9-26 days before being placed on study.

SHORT-TERM STUDIES

Single-Dose Study

Male and female F344/N rats and $B6C3F_1$ mice were observed for 7 days before the test began. Animals were approximately 5 weeks old when placed on study.

Groups of five males and five females of each species were administered single doses (0, 10, 50, 100, 500, or 1,000 mg/kg) of pentachloroethane in corn oil by gavage. Surviving animals were killed on day 14.

Rats were housed individually and mice were housed five per cage. All animals received water and feed *ad libitum* during the observation period. Details of animal maintenance are presented in Table 2.

Animals were observed for mortality. Necropsies were performed on all animals. Animals were weighed on the day of dosing and on day 7 and day 14.

Fourteen-Day Study

Three- to four-week-old male and female F344/N rats and $B6C3F_1$ mice were obtained from Frederick Cancer Research Center and observed for 9 days (rats) or 26 days (mice).

Groups of five males and five females of each species were administered pentachloroethane (0, 10, 50, 100, 500, or 1,000 mg/kg) in corn oil by gavage for 14 days.

Rats were housed individually and mice were housed five per cage. All animals received water and feed *ad libitum*. Details of animal maintenance are presented in Table 2. Animals were observed daily for mortality and were weighed weekly. Necropsies were performed on all animals, and the lung, liver, and spleen were examined histologically.

Thirteen-Week Study

Thirteen-week studies were conducted to evaluate the cumulative toxicity of pentachloroethane and to determine the doses to be used in the 2-year studies.

Three-week-old male and female F344/N rats and $B6C3F_1$ mice were obtained from Frederick Cancer Research Center, observed for 2 weeks, and then assigned to test groups according to a table of random numbers.

Rats were housed individually in stainless steel wire mesh cages, and mice were housed five per cage in polypropylene cages covered with nonwoven polyester filter bonnets (Table 2). Racks and filters were changed once every 2 weeks. Cages, bedding, and water bottles were replaced twice per week.

Groups of 10 rats of each sex were administered pentachloroethane (5, 10, 50, 125, or 250 mg/kg) in corn oil by gavage, 5 days per week, for 13 weeks. Groups of 10 mice of each sex were administered 5, 10, 50, 100, or 500 mg/kg in corn oil by gavage on the same schedule. Vehicle controls received only corn oil.

Animals were checked for mortality and morbidity twice daily. Animals that were judged moribund were killed and necropsied. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Animals were group weighed at weekly intervals.

At the end of the 13-week study, survivors were killed with carbon dioxide, and necropsies were performed on all animals, unless precluded in whole or in part by autolysis or cannibalization. The following specimens were examined for control and high-dose animals: brain, pituitary, thyroid, parathyroid, esophagus, trachea, adrenal, liver, lung, kidney, spleen, salivary gland, lymph nodes (mandibular, mesenteric), pancreas, heart, testes, epididymis, prostate, seminal vesicle, ovary, uterus, vagina, urinary bladder, stomach, duodenum, colon, skin, mammary tissue, bone marrow, gallbladder (mice), and spinal cord. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats of each sex were administered 75 and 150 mg/kg pentachloroethane in corn oil by gavage, five times per week, for 103 weeks and observed for 0-1 week. Similar groups of mice received 250 or 500 mg/kg on the same schedule. Groups of 50 rats and 50 mice of each sex received corn oil alone five times per week and served as vehicle controls (Table 2).

Source and Specifications of Test Animals

Four-week-old male and female F344/N rats and 5-week-old male and female $B6C3F_1$ mice were obtained from Charles River Breeding Laboratories (Portage, MI), observed for 3 weeks, and assigned to cages according to a table of random numbers. Another table of random numbers was used to assign cages to control and dosed groups.

Animal Maintenance

Rats and mice were housed five per cage in polycarbonate cages covered with bonded, spun fiberglass filters (Table 2). Racks and filters were changed once every 2 weeks. Cages and bedding were replaced twice per week. Feed and city tap water (via an automatic watering system) were available *ad libitum*.

The temperature in the animal rooms was 23° ± 4°C and the humidity was 40%-70%. Room air was changed 12 times per hour. Fluorescent lighting provided illumination 12 hours per day.

All animals were housed in the same room; no other chemicals were on test in that room.

Dosage Preparation

Pentachloroethane was weighed and mixed with corn oil (Table 2) to give the desired concentration. Rats received 5 ml/kg and mice 10 ml/kg body weight. Pentachloroethane/corn oil mixtures were stored at 4°C for no longer than 7 days.

Pentachloroethane/corn oil mixtures were analyzed at Midwest Research Institute and found to be stable at room temperatures for up to 7 days (Appendix G). Blindly selected samples of pentachloroethane in corn oil were analyzed periodically (Appendix H).

Clinical Examinations and Pathology

All animals were observed three times daily for signs of toxicity. Clinical signs were recorded monthly. Body weights by cage were recorded approximately every 2 weeks. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. Animals were killed with carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction, thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary, and spinal cord.

Necropsies were performed on all animals, unless precluded in whole or in part by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Neoplastic nodules were classified according to the recommendations of Squire and Levitt (1975) and the National Academy of Sciences (1980). When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechniques were evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10 percent of the animals were evaluated by an experienced rodent pathologist. Slides of all target tissues and those on which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative slides

selected by the PWG Chairperson were reviewed blindly by the PWG's experienced rodent pathologists, who reached a consensus and compared their findings with the original diagnoses. When conflicts were found, the PWG sent the appropriate slides and their comments to the original pathologist for review. (This procedure is described, in part, by Maronpot and Boorman, in press.) The final diagnosis represents a consensus of contractor pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) extensions of Cox's methods for testing for a dose-related trend.

The incidence of neoplastic or nonneoplastic lesions has been given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

For the statistical analysis of tumor incidence data, two different methods of adjusting for intercurrent mortality were employed. Each used the classical methods for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high- and low-dose groups with controls and tests for overall dose-response trends.

The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal;" i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel methods to obtain an overall P-value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972) and of Tarone (1975).

The second method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "incidental"; i.e., they were merely observed at autopsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in dosed and control groups were compared in each of five time intervals: 0-52 weeks, 53-78 weeks, 79-92 weeks, week 93 to the week before the terminal kill period, and the terminal kill period. The denominators of these proportions were the number of animals actually autopsied during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980, for the computational details of both methods.)

In addition to these tests, one other set of statistical analyses was used and reported in the tables analyzing primary tumors: the Fisher's exact test for pairwise comparisons and the Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). These tests were based on the overall proportion of tumor-bearing animals. All reported P values are one-sided.

For studies in which there is little effect of compound administration on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death.

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS

	Single-Dose Study	14-Day Study	13-Week Study	2-Year Study *(a)*
Experimental Design				
Size of Test Groups	5 males and 5 females of each species.	5 males and 5 females of each species.	10 males and 10 females of each species.	50 males and 50 females of each species.
Doses	Rats and mice: 0, 10, 50, 100, 500, or 1,000 mg/kg body weight pentachloroethane in corn oil; Vehicle control groups: Lou Ana brand corn oil (Lou Ana Co., Opelousas, LA)	Same as single-dose study	Rats: 5, 10, 50, 125, or 250 mg/kg body weight pentachloroethane in corn oil; Mice: 5, 10, 50, 100, or 500 mg/kg body weight pentachloroethane in corn oil; Vehicle control groups: Lou Ana brand corn oil (Lou Ana Co., Opelousas, LA)	Rats: 75 or 150 mg/kg body weight pentachloroethane in corn oil; Mice: 250 or 500 mg/kg body weight pentachloroethane in corn oil; Vehicle control groups: Lou Ana brand corn oil (Lou Ana Co., Opelousas, LA)
Duration of Dosing	Single dose	Daily for 14 days	5 days per week for 13 weeks	5 days per week for 103 weeks *(b)*
Type and Frequency of Observation	Observed daily for mortality	Same as single-dose study	Observed twice daily for mortality and morbidity	Observed three times daily for mortality and morbidity
Necropsy and Histological Examination	Necropsies performed on all animals;	Necropsies performed on all animals; lung, liver, and spleen examined histologically	Necropsies performed on all animals. Histopathologic examination performed on all control animals and all animals of the highest dose group of each sex and species	Necropsies and histological examination of tissues performed on all animals
Animals and Animal Maintenance				
Species	F344/N rats; $B6C3F_1$ mice	F344 rats/N; $B6C3F_1$ mice	F344/N rats; $B6C3F_1$ mice	F344/N rats; $B6C3F_1$ mice
Animal Source	Frederick Cancer Research Center (Frederick, MD)	Same as single-dose study	Same as single-dose study	Charles River Breeding Laboratories (Portage, MI)
Time Held Before Start of Test	7 days	Rats: 9 days; Mice: 26 days	14 days	22 days
Age When Placed On Study	Rats: 4-5 weeks old	Rats: 4-5 weeks old; Mice: 7-8 weeks old	5-6 weeks old	Rats: 7 weeks; Mice: 8 weeks
Method of Animal Distribution	Assigned to cages according to a table of random numbers and then to dosed and control groups according to a second table of random numbers	Distributed to cages by weight so that each dose group had animals of approximately the same average weight	Same as single-dose study	Same as single-dose study

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS (Continued)

	Single-Dose Study	14-Day Study	13-Week Study	2-Year Study *(a)*
Feed	Wayne® Lab Blox (Allied Mills, Chicago, IL); available *ad libitum*	Same as single-dose study	Same as single-dose study	Same as single-dose study
Bedding	Absorb-Dri® heat-treated hardwood chips (Lab Products, Inc., Garfield, NJ)	Same as single-dose study	Same as single-dose study	Same as single-dose study
Water	Tap water in glass bottles; stainless steel sipper tubes	Same as single-dose study	Same as single-dose study	Tap water; automatic watering system (Edstrom Industries, Inc., Waterford, WI)
Cages	Rats: steel wire mesh (Hoeltge Co., Cincinnati, OH); Mice: Polypropylene (Lab Products, Inc., Garfield, NJ)	Same as single-dose study	Same as single-dose study	Rats and mice: Polycarbonate (Lab Products, Inc., Garfield, NJ)
Animals per Cage	Rats: one Mice: five	Same as single-dose study	Same as single-dose study	Rats and mice: five
Cage Filters	Polyester filter bonnet (Lab Products, Inc., Garfield, NJ)	Same as single-dose study	Same as single-dose study	Bonded spun fiberglass (Lab Products, Inc., Garfield, NJ)
Animal Room Environment	23° ±4°C; humidity 40%-70%; 12 changes of room air per hour	Same as single-dose study	Same as single-dose study	Same as single-dose study
Chemical/Vehicle Mixture				
Preparation	Pentachloroethane was added to corn oil on a weight per volume basis	Same as single-dose study	Same as single-dose study	High-dose mixture prepared by adding pentachloroethane to corn oil on a weight per volume basis; low-dose mixture prepared by diluting high-dose mixture with corn oil
Maximum Storage Time	—	7 days	7 days	7 days
Storage Conditions	—	4°C	4°C	4°C

(a) Within each study, control and dosed animals were of the same strain, sex, and age range and from the same source and shipment. All animals shared the same room, and all aspects of animal care and maintenance were similar.

(b) All high-dose male mice were dead by week 41; all high-dose female mice were dead by week 74.

III. RESULTS

RATS

SHORT-TERM STUDIES

Single-Dose Study
Fourteen-Day Study
Thirteen-Week Study

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

MICE

SHORT-TERM STUDIES

Single-Dose Study
Fourteen-Day Study
Thirteen-Week Study

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

SHORT-TERM STUDIES

Single-Dose Study

The gavage doses employed in this experiment (0, 10, 50, 100, 500, and 1,000 mg/kg) were well tolerated by both sexes. Weight gains were comparable for control and dosed groups. A single control female rat died on day 1 as a result of a gavage error. No effects that could be attributed to pentachloroethane administration were observed at scheduled necropsy.

The apparent lack of acute toxicity observed in this experiment resulted in the selection of the same dosage levels for the 14-day study.

Fourteen-Day Study

The survival and body weight changes observed in this experiment are summarized in Table 3. Clear signs of toxicity were noted, with all animals dying that received the 1,000 mg/kg/day dose and 3/5 animals of each sex dying that received the 500 mg/kg/day dose. Three animals of each sex died within 24 hours of receiving the first dose of 1,000 mg/kg, while the remaining high-dose rats died on days 3 and 4. Deaths among the 500 mg/kg/day dosage groups occurred between days 4 and 10. No gross or microscopic lesions were detected in the animals that died on test. The only clinical sign observed was lethargy among the rats receiving the 500 and 1,000 mg/kg/day doses.

Body weight gains by animals receiving up to 100 mg/kg/day were similar to those of control rats. The two male and two female animals that survived the 500 mg/kg/day dosage regimen gained weight throughout the study; however, the males gained 29% less and the females gained 40% less than their respective controls. Final body weight differences for the 500 mg/kg/day dose groups were 10% (males) and 15% (females) less than those of controls. No compound-related gross changes were noted at necropsy, and microscopic lesions were not detected in liver, lungs, or spleen.

The findings of this study resulted in the selection of dosage levels of 5, 10, 50, 125, and 250 mg/kg/day for the 13-week study.

Thirteen-Week Study

The survival and body weight gains for rats receiving a daily administration of pentachloroethane 5 days per week for 13 weeks are summarized in Table 4. All animals survived the 13-week administration period, and no compound-related gross or histopathologic effects were observed. Body weight gains for rats receiving doses as high as 125 mg/kg/day were considered to be within normal limits. Body weight gains for animals receiving the 250 mg/kg/day dose were slightly depressed (10% for males and 17% for females); final body weights were 5% (males) and 9% (females) less than those of controls.

The body weight gain decrements noted at the 250 mg/kg/day dose and previous experience with chlorinated ethanes dictated the selection of doses of 75 and 150 mg/kg/day for the 2-year study in rats.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)			Body Weight Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALE					
0	5/5	81.0 ±1.76	147.4 ±6.55	+66.4 ±6.16	—
10	5/5	82.2 ±2.37	156.4 ±3.59	+74.2 ±4.83	+ 6
50	5/5	83.2 ±2.48	153.4 ±5.99	+70.2 ±7.25	+ 4
100	5/5	83.2 ±2.22	147.8 ±4.98	+64.6 ±3.99	0
500	2/5 *(d)*	85.5 ±4.50	132.5 ±1.50	+47.0 ±6.00	−10
1,000	0/5 *(e)*	*(f)*	*(f)*	*(f)*	
FEMALE					
0	5/5	75.8 ±1.66	112.6 ±2.16	+36.8 ±0.86	—
10	5/5	76.0 ±1.30	114.8 ±3.25	+38.8 ±3.99	+ 2
50	5/5	75.6 ±1.50	116.0 ±2.10	+40.4 ±1.57	+ 3
100	5/5	76.6 ±1.72	115.6 ±1.69	+39.0 ±1.05	+ 3
500	2/5 *(g)*	74.5 ±0.50	96.5 ±2.50	+22.0 ±2.00	−15
1,000	0/5 *(h)*	*(f)*	*(f)*	*(f)*	

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.

(b) Mean weight change of the survivors of the group ± standard error of the mean.

(c) Weight of the dosed survivors relative to the survivors of the controls =

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

(d) One animal died on day 4 and two on day 8.

(e) Three animals died on day 1 and two animals on day 4.

(f) No data are presented due to the 100% mortality in this group.

(g) Two animals died on day 9 and one on day 10.

(h) Three animals died on day 1 and two on day 3.

TABLE 4. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Body Weight Relative to Controls *(b)* (Percent)
		Initial	Final	Change	
MALE					
0	10/10	105	322	+217	—
5	10/10	110	321	+211	0
10	10/10	111	315	+204	−2
50	10/10	118	330	+212	+ 3
125	10/10	106	305	+199	−5
250	10/10	110	306	+196	−5
FEMALE					
0	10/10	103	196	+ 93	—
5	10/10	101	194	+ 93	−1
10	10/10	98	192	+ 94	−2
50	10/10	95	188	+ 93	−4
125	10/10	93	178	+ 85	−9
250	10/10	102	179	+ 77	−9

(a) Number surviving/number per group.

(b) Weight relative to controls =

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

TWO-YEAR STUDIES

Body Weights and Clinical Signs

The growth curves for rats administered pentachloroethane 5 days per week for 103 weeks by gavage are shown in Figure 1. Male rats administered either the 75 or 150 mg/kg/day dose maintained normal body weights through the first 76 weeks of the study. After this time, body weights of the dosed males tended to be slightly less than those of control animals. A dose-response relationship for this minimal effect was not evident.

Dosed females maintained normal body weights through the initial 42 weeks of the study. Although the females continued to gain weight throughout the remainder of the study, a decrement (ranging from 8% to 21% as compared with controls) was evident during the final 62 weeks. Final mean body weights were less than those of controls for dosed male rats (4%-5%) and for dosed female rats (8%-12%) (Appendix I, Table I1). As was the case among males, a dose-response relationship was not evident for this effect.

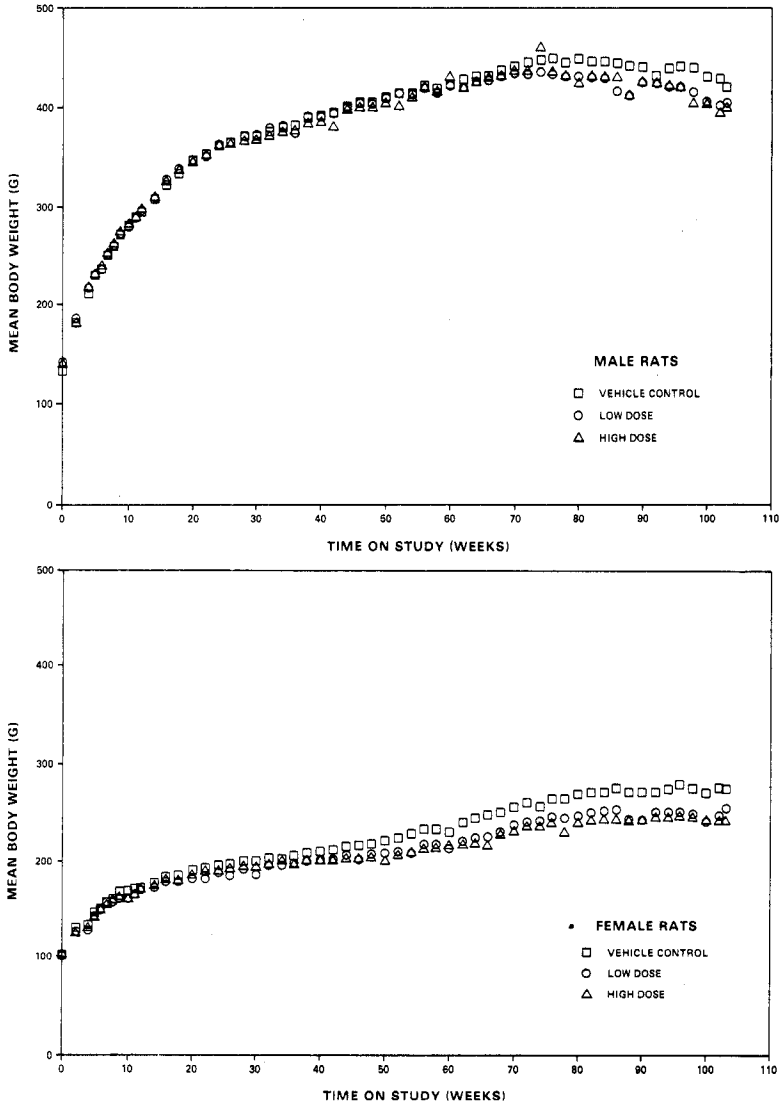

Figure 1. Growth Curves for Rats Administered Pentachloroethane by Gavage

Survival

Estimates of the probabilities of survival of male and female rats administered pentachloroethane, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 2. One high-dose male, one low-dose female, and two high-dose females were killed as a result of gavage errors during weeks 93, 103, 98, and 101, respectively. The administration of pentachloroethane had a dose-related adverse effect on the survival of rats. Among males, 82% of the controls, 66% of the low-dose, and 52% of the high-dose animals survived to the end of the study. In females, 76% of the controls, 72% of the low-dose, and 50% of the high-dose animals survived to the end of the study. The survival of both high-dose males and females was significantly less than that of their respective controls ($P < 0.01$ and $P < 0.05$, respectively). There was also evidence (P=0.058) of reduced survival in the low-dose male group, but no differences were observed between the survival of low-dose females and controls.

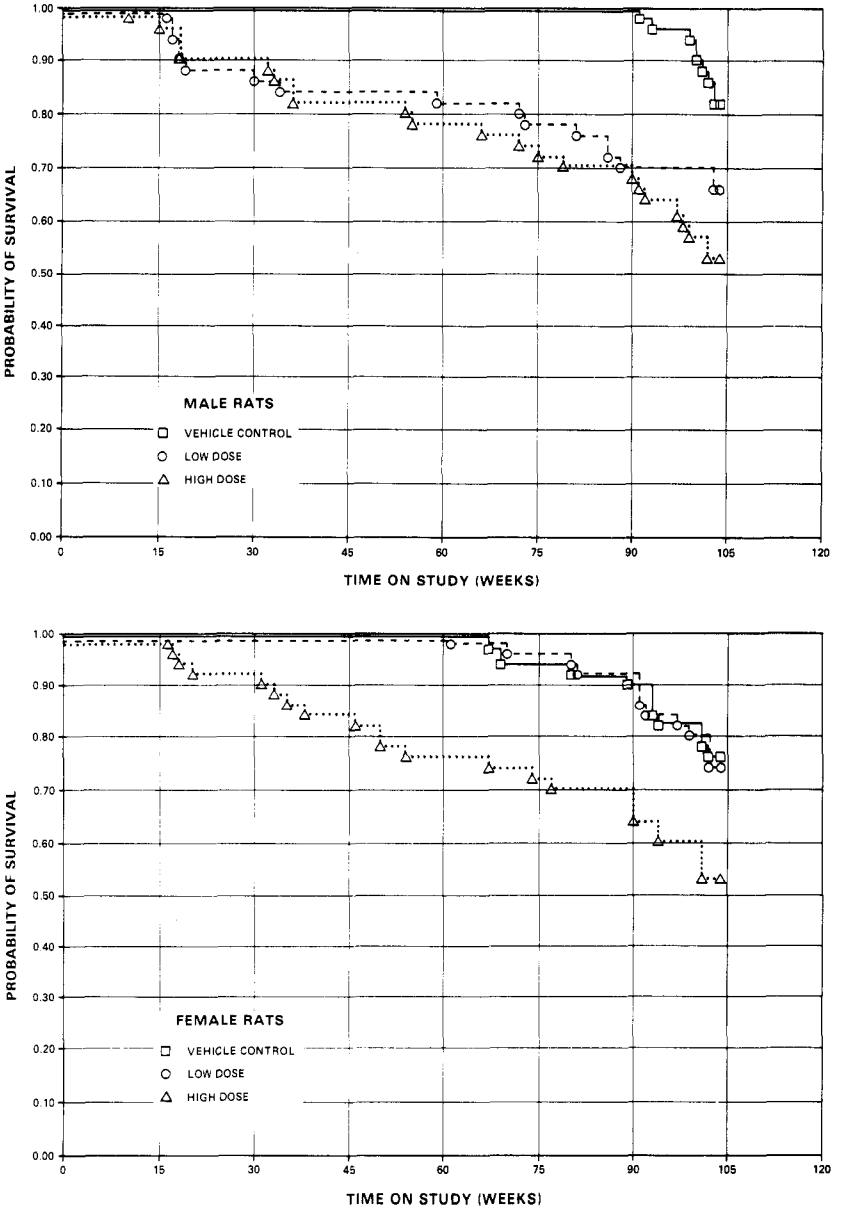

Figure 2. Survival Curves for Rats Administered Pentachloroethane by Gavage

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; the survival and tumor status for each individual animal in the male and female rat studies appear in Appendix A, Tables A3 and A4. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.

Tables 5 and 6 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Statistical analyses of the incidences of primary tumors in rats revealed primarily negative trends. Among females, a negative trend was observed in the incidence of pituitary adenomas (P=0.016, incidental tumor test). Among males, negative trends were observed in the incidences of subcutaneous tissue fibromas ($P<0.05$) and pituitary adenomas (primarily chromophobe) ($P<0.01$).

Kidney: Chronic, diffuse inflammation of the kidney (nephropathy) was observed at a significant ($P<0.001$) and dose-related, increased incidence in male rats (control, 4/50, 8%; low-dose, 14/49, 29%; high-dose, 33/50, 66%). The nephropathy was characterized by prominent interstitial fibrosis, interstitial accumulation of mononuclear inflammatory cells, and severe tubular dilation in the pars recta (inner cortex), with some dilated tubules containing giant cells and casts. The lesions could be distinguished from those seen in "aging" nephropathy (Barthold, 1979) where interstitial fibrosis and tubular dilation are not as severe as in this toxic lesion. In addition, the giant cells within tubules are not a feature of aging nephropathy. Glomerular hyalinization was also observed. Mineralization of the renal papilla was seen at a significantly increased incidence ($P<0.001$) in dosed male rats: controls, 4/50 (8%); low-dose, 29/49 (59%); high-dose, 29/50 (58%).[See on page 8 Note Added Subsequent to Peer Review.]

Lung: There was a significant (P=0.009) dose-related trend in the incidence of interstitial inflammation of the lung in male rats (control, 5/50, 10%; low-dose, 10/49, 20%; high-dose, 15/50, 30%). However, a higher incidence of acute/chronic inflammation was observed in controls than in the high-dose group (control, 27/50, 54%; low-dose, 31/49, 63%; high-dose, 19/50, 38%), and thus, an association between inflammation of the lung and pentachloroethane cannot be established.

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma			
Tumor Rates			
Overall *(b)*	5/50(10)	0/49(0)	0/50(0)
Adjusted *(c)*	11.5%	0.0%	0.0%
Terminal *(d)*	3/41(7)	0/33(0)	0/26(0)
Statistical Tests *(e)*			
Life Table	P=0.018N	P=0.059N	P=0.093N
Incidental Tumor Test	P=0.021N	P=0.109N	P=0.077N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.006N	P=0.030N	P=0.028N
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(b)*	2/50(4)	3/49(6)	3/50(6)
Adjusted *(c)*	4.7%	8.7%	10.0%
Terminal *(d)*	1/41(2)	2/33(6)	1/26(4)
Statistical Tests *(e)*			
Life Table	P=0.221	P=0.405	P=0.299
Incidental Tumor Test	P=0.243	P=0.224	P=0.337
Cochran-Armitage Trend, Fisher Exact Tests	P=0.412	P=0.490	P=0.500
***Kidney: Tubular-Cell Adenoma**			
Tumor Rates			
Overall *(a)*	0/50(0%)	1/49(2%)	4/50(8%)
Adjusted *(b)*	0.0%	3.0%	13.6%
Terminal *(c)*	0/41(0%)	1/33(3%)	2/26(8%)
Statistical Tests *(d)*			
Life Table	P=0.009	P=0.457	P=0.024
Incidental Tumor Test	P=0.020	P=0.457	P=0.055
Cochran-Armitage Trend, Fisher Exact Tests	P=0.026	P=0.495	P=0.059
Kidney: Tubular-Cell Adenoma or Adenocarcinoma *(f)			
Tumor Rates			
Overall *(a)*	1/50(2)%	2/49(4%)	4/50(8%)
Adjusted *(b)*	2.4%	5.8%	13.6%
Terminal *(c)*	1/41(2%)	1/33(3%)	2/26(8%)
Statistical Tests *(d)*			
Life Table	P=0.047	P=0.426	P=0.077
Incidental Tumor Test	P=0.083	P=0.306	P=0.145
Cochran-Armitage Trend, Fisher Exact Tests	P=0.119	P=0.492	P=0.181
Pituitary: Chromophobe Adenoma			
Tumor Rates			
Overall *(b)*	20/48(42)	10/46(22)	3/46(7)
Adjusted *(c)*	45.0%	31.9%	11.6%
Terminal *(d)*	16/40(40)	9/30(30)	2/23(9)
Statistical Tests *(e)*			
Life Table	P=0.004N	P=0.152N	P=0.007N
Incidental Tumor Test	P=0.001N	P=0.135N	P=0.002N
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001N	P=0.032N	P<0.001N

*See on page 8 Note Added Subsequent to Peer Review

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (Continued) *(a)*

	Vehicle Control	Low Dose	High Dose
Pituitary: All Adenomas			
Tumor Rates			
Overall *(b)*	23/48(48)	13/46(28)	4/46(9)
Adjusted *(c)*	52.0%	40.1%	14.0%
Terminal *(d)*	19/40(48)	11/30(37)	2/23(9)
Statistical Tests *(e)*			
Life Table	P=0.004N	P=0.212N	P=0.005N
Incidental Tumor Test	P<0.001N	P=0.151N	P<0.001N
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001N	P=0.040N	P<0.001N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	3/49(6)	1/48(2)	4/50(8)
Adjusted *(c)*	7.3%	3.1%	12.4%
Terminal *(d)*	3/41(7)	1/32(3)	1/26(4)
Statistical Tests *(e)*			
Life Table	P=0.238	P=0.397N	P=0.288
Incidental Tumor Test	P=0.441	P=0.397N	P=0.608
Cochran-Armitage Trend, Fisher Exact Tests	P=0.422	P=0.316N	P=0.511
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	6/50(12)	6/45(13)	3/46(7)
Adjusted *(c)*	14.6%	17.6%	10.6%
Terminal *(d)*	6/41(15)	4/31(13)	2/25(8)
Statistical Tests *(e)*			
Life Table	P=0.485N	P=0.425	P=0.517N
Incidental Tumor Test	P=0.348N	P=0.439	P=0.404N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.246N	P=0.543	P=0.287N
Pancreatic Islets: Islet-Cell Adenoma			
Tumor Rates			
Overall *(b)*	4/48(8)	5/48(10)	0/50(0)
Adjusted *(c)*	9.5%	14.6%	0.0%
Terminal *(d)*	3/41(7)	4/33(12)	0/26(0)
Statistical Tests *(e)*			
Life Table	P=0.181N	P=0.372	P=0.139N
Incidental Tumor Test	P=0.155N	P=0.262	P=0.115N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.064N	P=0.500	P=0.054N
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	5/48(10)	5/48(10)	1/50(2)
Adjusted *(c)*	11.9%	14.6%	3.8%
Terminal *(d)*	4/41(10)	4/33(12)	1/26(4)
Statistical Tests *(e)*			
Life Table	P=0.337N	P=0.494	P=0.240N
Incidental Tumor Test	P=0.207N	P=0.383	P=0.211N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.082N	P=0.630	P=0.093N

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (Continued) *(a)*

	Vehicle Control	Low Dose	High Dose
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	41/49(84)	34/47(72)	33/49(67)
Adjusted *(c)*	91.0%	94.4%	94.3%
Terminal *(d)*	36/40(90)	31/33(94)	24/26(92)
Statistical Tests *(e)*			
Life Table	P=0.044	P=0.548	P=0.060
Incidental Tumor Test	P=0.113	P=0.381	P=0.209
Cochran-Armitage Trend, Fisher Exact Tests	P=0.041N	P=0.137N	P=0.049N

(a) Dosed groups received doses of 75 or 150 mg/kg of pentachloroethane by gavage.

(b) Number of tumor bearing animals/number of animals examined at the site.

(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.

(d) Observed tumor incidence at terminal kill.

(e) Beneath the control incidence are the P-values associated with the trend test. Beneath each dosed group incidence is the P-value corresponding to the pairwise comparison between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher's exact test compare directly the overall incidence rates. A negative trend is indicated by (N).

(f) The incidences of tubular-cell adenomas and adenocarcinomas in male rats were determined by the Pathology Working Group after the preparation of a second set of histopathology slides. This was necessitated by the inadvertent destruction of the original slides.

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	1/49(2)	3/49(6)	1/48(2)
Adjusted *(c)*	2.4%	7.5%	3.1%
Terminal *(d)*	0/38(0)	1/36(3)	0/25(0)
Statistical Tests *(e)*			
Life Table	P=0.484	P=0.304	P=0.690
Incidental Tumor Test	P=0.598N	P=0.290	P=0.735N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.603	P=0.309	P=0.747
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(b)*	1/49(2)	4/49(8)	2/48(4)
Adjusted *(c)*	2.6%	9.8%	5.9%
Terminal *(d)*	1/38(3)	2/36(6)	0/25(0)
Statistical Tests *(e)*			
Life Table	P=0.275	P=0.177	P=0.395
Incidental Tumor Test	P=0.380	P=0.232	P=0.516
Cochran-Armitage Trend, Fisher Exact Tests	P=0.397	P=0.181	P=0.492
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	2/49(4)	5/49(10)	2/48(4)
Adjusted *(c)*	5.0%	12.1%	5.9%
Terminal *(d)*	1/38(3)	2/36(6)	0/25(0)
Statistical Tests *(e)*			
Life Table	P=0.419	P=0.217	P=0.575
Incidental Tumor Test	P=0.589	P=0.261	P=0.671N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.573	P=0.218	P=0.684
Liver: Neoplastic Nodule or Carcinoma			
Tumor Rates			
Overall *(b)*	1/49(2)	3/48(6)	0/45(0)
Adjusted *(c)*	2.6%	8.1%	0.0%
Terminal *(d)*	1/38(3)	2/35(6)	0/22(0)
Statistical Tests *(e)*			
Life Table	P=0.536N	P=0.287	P=0.609N
Incidental Tumor Test	P=0.488N	P=0.285	P=0.609N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.405N	P=0.301	P=0.521N
Pituitary: Chromophobe Adenoma			
Tumor Rates			
Overall *(b)*	23/49(47)	14/46(30)	12/45(27)
Adjusted *(c)*	53.1%	33.3%	40.4%
Terminal *(d)*	18/38(47)	8/34(24)	7/24(29)
Statistical Tests *(e)*			
Life Table	P=0.204N	P=0.104N	P=0.288N
Incidental Tumor Test	P=0.075N	P=0.021N	P=0.133N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.025N	P=0.075N	P=0.034N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (Continued) *(a)*

	Vehicle Control	Low Dose	High Dose
Pituitary: All Adenomas			
Tumor Rates			
Overall *(b)*	27/49(55)	17/46(37)	12/45(27)
Adjusted *(c)*	59.6%	41.0%	40.4%
Terminal *(d)*	20/38(53)	11/34(32)	7/24(29)
Statistical Tests *(e)*			
Life Table	P=0.080N	P=0.094N	P=0.121N
Incidental Tumor Test	P=0.016N	P=0.029N	P=0.028N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.004N	P=0.058N	P=0.005N
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	4/46(9)	3/48(6)	2/45(4)
Adjusted *(c)*	10.5%	7.8%	8.3%
Terminal *(d)*	3/35(9)	2/35(6)	2/24(8)
Statistical Tests *(e)*			
Life Table	P=0.417N	P=0.497N	P=0.513N
Incidental Tumor Test	P=0.347N	P=0.341N	P=0.455N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.271N	P=0.476N	P=0.349N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	9/49(18)	8/49(16)	10/48(21)
Adjusted *(c)*	23.0%	19.6%	34.5%
Terminal *(d)*	8/38(21)	5/36(14)	7/25(28)
Statistical Tests *(e)*			
Life Table	P=0.156	P=0.532N	P=0.170
Incidental Tumor Test	P=0.242	P=0.431N	P=0.238
Cochran-Armitage Trend, Fisher Exact Tests	P=0.429	P=0.500N	P=0.480
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	7/45(16)	12/48(25)	2/40(5)
Adjusted *(c)*	17.8%	29.5%	8.0%
Terminal *(d)*	6/38(16)	8/36(22)	2/25(8)
Statistical Tests *(e)*			
Life Table	P=0.297N	P=0.141	P=0.221N
Incidental Tumor Test	P=0.235N	P=0.169	P=0.209N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.135N	P=0.192	P=0.109N
Uterus: Endometrial Stromal Polyp or Sarcoma			
Tumor Rates			
Overall *(b)*	9/45(20)	12/48(25)	2/40(5)
Adjusted *(c)*	23.0%	29.5%	8.0%
Terminal *(d)*	8/38(21)	8/36(22)	2/25(8)
Statistical Tests *(e)*			
Life Table	P=0.158N	P=0.283	P=0.109N
Incidental Tumor Test	P=0.114N	P=0.330	P=0.102N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.053N	P=0.372	P=0.039N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (Continued) *(a)*

(a) Dosed groups received doses of 75 or 150 mg/kg of pentachloroethane by gavage.

(b) Number of tumor-bearing animals/number of animals examined at the site (percent).

(c) Kaplan-Meier estimated lifetime tumor incidence (percent) after adjusting for intercurrent mortality.

(d) Observed tumor incidence in surviving animals killed at the end of the study.

(e) Beneath the control incidence are the P-values associated with the trend test. Beneath each dosed group incidence is the P-value corresponding to the pairwise comparison between that dosed group and the controls. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage trend and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

SHORT-TERM STUDIES

Single-Dose Study

The gavage doses employed in this experiment (0, 10, 50, 100, 500, or 1,000 mg/kg) were well tolerated by both sexes of mice. All animals survived to the end of the experiment (14 days) and no compound-related effects were observed at necropsy. Since control mice lost weight, weight changes in dosed mice were uninterpretable. The lack of acute toxicity in this experiment resulted in the selection of the same dosage levels for the 14-day study.

Fourteen-Day Study

The survival and body weight changes in mice receiving gavage doses of pentachloroethane for 14 days are summarized in Table 7. A single female mouse in the 1,000 mg/kg/day group died on day 2 of the experiment and the surviving animals at this dose exhibited a slight weight loss. Females receiving doses from 50 to 500 mg/kg/day exhibited weight gain decrements from 25% to 50%, but these decrements were not dose-related. Pentachloroethane administration did not appear to decrease weight gains in male mice. No compound-related changes were observed at group necropsy, and microscopic lesions were not detected in liver, lungs, or spleen.

Dosage selection for the 13-week study was made on the basis of the one death and marked body weight gain decrements among the female mice receiving the 1,000 mg/kg/day dose. The doses selected were 0, 5, 10, 50, 100, and 500 mg/kg/day for both sexes.

TABLE 7. SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)			Body Weight Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALE					
0	5/5	26.8 ±0.58	27.0 ±0.71	+0.2 ±1.24	—
10	5/5	25.0 ±0.32	26.2 ±1.32	+1.2 ±1.07	−3
50	5/5	26.0 ±0.84	27.6 ±0.98	+1.6 ±0.68	+2
100	5/5	22.8 ±1.20	26.8 ±1.11	+4.0 ±2.00	−1
500	5/5	25.8 ±1.53	26.8 ±1.39	+1.0 ±0.31	−1
1,000	5/5	27.4 ±2.11	29.0 ±0.55	+1.6 ±1.60	+7
FEMALE					
0	5/5	17.8 ±1.16	21.0 ±0.32	+3.2 ±0.97	—
10	5/5	18.6 ±0.93	21.6 ±0.51	+3.0 ±1.26	+3
50	5/5	20.6 ±0.68	22.2 ±0.58	+1.6 ±0.24	+6
100	5/5	19.4 ±0.24	21.8 ±0.37	+2.4 ±0.24	+4
500	5/5	19.2 ±0.37	21.6 ±0.24	+2.4 ±0.51	+3
1,000	4/5 *(d)*	19.8 ±0.25	19.5 ±1.55	−0.3 ±1.60	−7

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.

(b) Mean weight of the survivors of the group ± standard error of the mean.

(c) Weight of the dosed survivors relative to the survivors of the controls =

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

(d) Death occurred on day 2.

Thirteen-Week Study

The survival and body weight gains for mice receiving daily gavage doses of pentachloroethane for 13 weeks are summarized in Table 8. All male mice survived the compound administration, and their body weight gains were comparable with those of controls. One female mouse administered the 500 mg/kg/day dose died during week 13, and the mean body weight gain in that group was depressed by 29%, relative to the controls.

No compound-related gross or microscopic lesions were detected among the mice in this study. Although one female receiving the 500 mg/kg/day dose died during the final week of the study, the lack of either gross or microscopic signs of toxicity and the variability of effects on body weight appeared to justify the selection of doses of 250 and 500 mg/kg/day for the 2-year study in mice.

TABLE 8. SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Body Weight Relative to Controls *(b)* (Percent)
		Initial	Final	Change	
MALE					
0	10/10	22	33	+11	—
5	10/10	22	35	+13	+6
10	10/10	22	34	+12	+3
50	10/10	22	33	+11	0
100	10/10	22	33	+11	0
500	10/10	22	33	+11	0
FEMALE					
0	10/10	18	25	+ 7	—
5	10/10	19	25	+ 6	0
10	10/10	18	25	+ 7	0
50	10/10	18	25	+ 7	0
100	10/10	18	24	+ 6	−4
500	9/10 *(c)*	18	23	+ 5	−8

(a) Number surviving/number per group.

(b) Weight relative to controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

(c) Death occurred during week 13.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

The growth curves for mice administered pentachloroethane in the chronic study are shown in Figure 3. Both dosage levels of pentachloroethane significantly depressed body weight gain in both sexes, but the males were affected earlier (Appendix I, Table I2). By week 12, the high-dose males had stopped growing appreciably, and by week 52, the body weights of the low-dose males were lower than those of controls. Between weeks 42 and 104, the low-dose males' mean body weight decreased by approximately 30%, while that of the controls remained essentially constant.

Mean body weights of high- and low-dose female mice were lower than that of controls after weeks 26 and 72, respectively. Between weeks 26 and 74 (when the last high-dose female died) the mean body weight of the high-dose females remained relatively constant. After weeks 75-80 body weights of low-dose females were lower than those of controls (>10%).

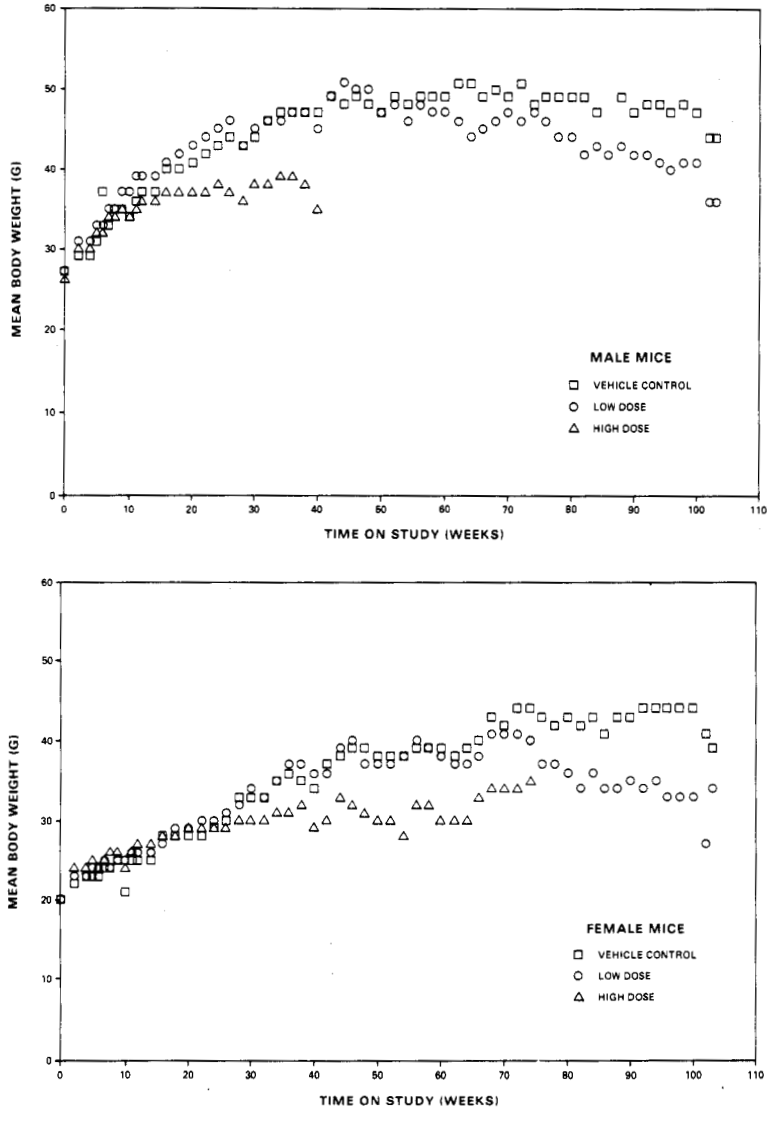

Figure 3. Growth Curves for Mice Administered Pentachloroethane by Gavage

Survival

Estimates of the probabilities of survival for male and female mice administered pentachloroethane, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 4.

The administration of pentachloroethane had a significant ($P < 0.01$) and dose-related adverse effect on the survival of both male and female mice. Among the high-dose males, the initial death was during week 18, and by week 41, 42/50 (84%) of the high-dose males had died. The 8 remaining high-dose males were killed during week 41, and 25 control males were killed during week 44 to provide control histopathological samples. Of the remaining control male mice, 19/25 (76%) survived to the end of the study. The initial death among the low-dose males occurred during week 31, and 22/50 (44%) of the low-dose males survived to the end of the study.

High-dose female mice survived the daily administration of pentachloroethane slightly longer than did the high-dose males. The initial high-dose female death occurred during week 38, and all of the animals were dead by week 74. Among the low-dose females, the initial death did not occur until week 53, but only 9/50 (18%) of the animals survived to the end of the study. Among the vehicle control female mice, 38/50 (76%) survived to the end of the study. One female control was accidentally killed during week 98.

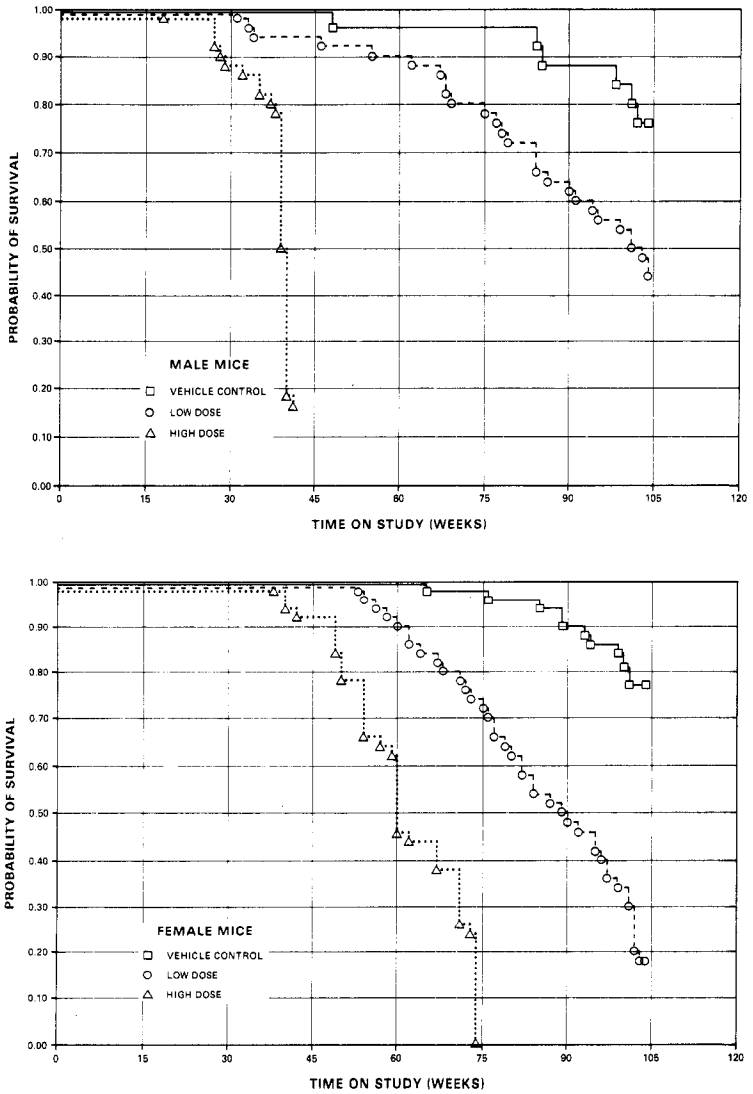

Figure 4. Survival Curves for Mice Administered Pentachloroethane by Gavage

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Tables 9 and 10 and Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status of each individual animal in the male and female mouse studies. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.

Tables 9 and 10 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

The markedly reduced survival observed in the high-dose male mice and the killing of 25 male controls at week 44 precluded the use of the usual statistical methods for these data. Observed tumor incidences in male mice were compared at 0-52 weeks, 53-103 weeks, and at terminal kill. The individual time interval comparisons were then combined by Mantel-Haenszel methods (1959) to obtain an overall result. The analyses of primary tumors in female mice were carried out by the procedures previously described. However, because there was little overlapping survival in the high-dose female and control groups, it was not feasible to compare these two groups by the incidental tumor test.

Liver: The incidence of hepatocellular carcinomas in dosed female mice was significantly increased ($P < 0.001$) relative to controls (controls, 1/46, 2%; low-dose, 28/42, 67%; high-dose, 13/45, 29%). A significantly increased ($P < 0.001$) incidence of hepatocellular carcinoma was also observed in low-dose male mice (controls, 4/48, 8%, low-dose, 26/44, 59%; high-dose, 7/45, 16%). Early mortality of high-dose male mice precluded an evaluation of their lifetime incidence of hepatocellular carcinoma. There was a significant ($P < 0.05$) increase in incidence over that observed among 25 controls killed at week 44. Carcinomas had areas of trabecular formations. These tumors metastasized to the lung in one low-dose female, two low-dose males, and one male control. There was also a significant ($P < 0.001$) dose-related increase in hepatocellular adenomas observed in female mice (controls, 2/46, 4%; low-dose, 8/42, 19%; high-dose, 19/45, 42%). Fatty metamorphosis occurred in increased incidences in dosed mice, but this effect was minimal and may reflect variability in nutritional status rather than a direct effect of the administration of pentachloroethane.

TABLE 9. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates *(b)*			
Overall	3/47(6)	4/41(10)	0/44(0)
0-52 weeks	2/24(8)	0/1(0)	0/44(0)
53-103 weeks	0/4 (0)	1/16(6)	0/0
terminal kill	1/19(5)	3/24(12)	0/0
Statistical Significance *(c)*	P=0.255N	P=0.359	P=0.118N
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates *(b)*			
Overall	3/47(6)	1/41(2)	0/44(0)
0-52 weeks	0/24(0)	0/1(0)	0/44(0)
53-103 weeks	1/4(25)	0/16(0)	0/0
terminal kill	2/19(11)	1/24(4)	0/0
Statistical Significance *(c)*	P=0.147N	P=0.147N	P=1.000
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates *(b)*			
Overall	6/47(13)	5/41(12)	0/44(0)
0-52 weeks	2/24(8)	0/1(0)	0/44(0)
53-103 weeks	1/4(25)	1/16(6)	0/0
terminal kill	3/19(16)	4/24(17)	0/0
Statistical Significance *(c)*	P=0.085N	P=0.475N	P=0.118N
Circulatory System: Hemangioma			
Tumor Rates *(b)*			
Overall	3/48(6)	4/44(9)	0/45(0)
0-52 weeks	0/25(0)	0/2(0)	0/45(0)
53-103 weeks	0/4(0)	2/18(11)	0/0
terminal kill	3/19(16)	2/24(8)	0/0
Statistical Significance *(c)*	P=0.525N	P=0.525N	P=1.000
Circulatory System: Hemangioma or Hemangiosarcoma			
Tumor Rates *(b)*			
Overall	3/48(6)	5/44(11)	0/45(0)
0-52 weeks	0/25(0)	0/2(0)	0/45(0)
53-103 weeks	0/4(0)	2/18(11)	0/0
terminal kill	3/19(16)	3/24(12)	0/0
Statistical Significance *(c)*	P=0.650	P=0.650	P=1.000
Liver: Adenoma			
Tumor Rates *(b)*			
Overall	10/48(21)	4/44(9)	7/45(16)
0-52 weeks	5/25(20)	0/2(0)	7/45(16)
53-103 weeks	0/4(0)	2/18(11)	0/0
terminal kill	5/19(26)	2/24(8)	0/0
Statistical Significance *(c)*	P=0.235N	P=0.162N	P=0.444N
Liver: Carcinoma			
Tumor Rates *(b)*			
Overall	4/48(8)	26/44(59)	7/45(16)
0-52 weeks	0/25(0)	1/2(50)	7/45(16)
53-103 weeks	0/4(0)	9/18(50)	0/0
terminal kill	4/19(21)	16/24(67)	0/0
Statistical Significance *(c)*	P<0.001	P<0.001	P=0.049

TABLE 9. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Liver: Adenoma or Carcinoma			
Tumor Rates *(b)*			
Overall	14/48(29)	30/44(68)	14/45(31)
0-52 weeks	5/25(20)	1/2(50)	14/45(31)
53-103 weeks	0/4(0)	11/18(61)	0/0
terminal kill	9/19(47)	18/24(75)	0/0
Statistical Significance *(c)*	P=0.026	P=0.005	P=0.237
Stomach: Squamous Cell Papilloma			
Tumor Rates *(b)*			
Overall	0/46(0)	3/37(8)	0/40(0)
0-52 weeks	0/25(0)	0/1(0)	0/40(0)
53-103 weeks	0/4(0)	1/12(8)	0/0
terminal kill	0/19(0)	2/24(8)	0/0
Statistical Significance *(c)*	P=0.249	P=0.249	P=1.000

(a) Dosed groups received doses of 250 or 500 mg/kg of pentachloroethane by gavage.

(b) Number of tumor-bearing animals/number of animals examined at the site (percent).

(c) Beneath the control incidence are the P-values associated with the trend test. Beneath each dosed group incidence is the P-value corresponding to the pairwise comparison between that dosed group and the controls. A negative trend is indicated by N.

TABLE 10. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Adenoma			
Tumor Rates			
Overall *(b)*	3/46(7)	0/41(0)	3/41(7)
Adjusted *(c)*	8.1%	0.0%	25.0%
Terminal *(d)*	3/37(8)	0/9(0)	0/0
Statistical Tests *(e)*			
Life Table	P=0.015	P=0.449N	P=0.004
Incidental Tumor Test	P=0.493	P=0.449N	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.554	P=0.143N	P=0.605
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/46(9)	0/41(0)	3/41(7)
Adjusted *(c)*	10.8%	0.0%	25.0%
Terminal *(d)*	4/37(11)	0/9(0)	0/0
Statistical Tests *(e)*			
Life Table	P=0.024	P=0.356N	P=0.004
Incidental Tumor Test	P=0.556	P=0.356N	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.458N	P=0.073N	P=0.565N
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	9/48(19)	2/43(5)	3/45(7)
Adjusted *(c)*	20.8%	12.2%	25.0%
Terminal *(d)*	4/38(11)	0/9(0)	0/0
Statistical Tests *(e)*			
Life Table	P=0.063	P=0.415N	P=0.003
Incidental Tumor Test	P=0.091N	P=0.007N	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.382N	P=0.038N	P=0.075N
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	2/46(4)	8/42(19)	19/45(42)
Adjusted *(c)*	5.4%	44.6%	60.9%
Terminal *(d)*	2/37(5)	3/9(33)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P<0.001	P<0.001
Incidental Tumor Test	P=0.060	P=0.023	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001	P=0.032	P<0.001
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	1/46(2)	28/42(67)	13/45(29)
Adjusted *(c)*	2.7%	84.6%	67.7%
Terminal *(d)*	1/37(3)	5/9(56)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P<0.001	P<0.001
Incidental Tumor Test	P=0.005	P<0.001	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.004	P<0.001	P<0.001

TABLE 10. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (Continued) *(a)*

	Vehicle Control	Low Dose	High Dose
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/46(7)	36/42(86)	32/45(71)
Adjusted *(c)*	8.1%	96.8%	93.6%
Terminal *(d)*	3/37(8)	8/9(89)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P<0.001	P<0.001
Incidental Tumor Test	P<0.001	P<0.001	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001	P<0.001	P<0.001
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	5/35(14)	3/29(10)	1/32(3)
Adjusted *(c)*	19.2%	57.1%	10.0%
Terminal *(d)*	5/26(19)	2/4(50)	0/0
Statistical Tests *(e)*			
Life Table	P=0.009	P=0.065	P=0.257
Incidental Tumor Test	P=0.115	P=0.148	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.089N	P=0.466N	P=0.120N

(a) Dosed groups received doses of 250 or 500 mg/kg of pentachloroethane by gavage.

(b) Number of tumor-bearing animals/number of animals examined at the site (percent).

(c) Kaplan-Meier estimated lifetime tumor incidence (percent) after adjusting for intercurrent mortality.

(d) Observed tumor incidence in surviving animals killed at the end of the study.

(e) Beneath the control incidence are the P-values associated with the trend test. Beneath each dosed group incidence is the P-value corresponding to the pairwise comparison between that dosed group and the controls. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage trend and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

(f) The configuration of survival and time of observation of tumor precludes the use of this statistic.

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

Despite a relatively cautious approach to the selection of dosage levels for the 2-year study, both rats and mice exhibited reduced survival due to compound-related toxicity. Neither gross observations nor histopathological evaluations revealed a specific cause or causes of decreased survival. The compound-related body weight decrements, especially for mice, and early deaths among dosed animals are evidence of a cumulative toxic effect of pentachloroethane in these species. A cumulative effect is consistent with pentachloroethane metabolism and excretion data presented by Yllner (1971). After a subcutaneous dose of 1,100-1,800 mg/kg, NMRI mice excreted only 55%, 80%, and 86% of the dose (as metabolites and parent compound) in 24, 48, and 72 hours, respectively. Further, quantifiable amounts of tri- and tetrachloroethylene, as well as parent compound, were excreted as long as 48 hours after treatment.

The results of the present study are similar to those of earlier bioassays of chloroethanes and chloroethylenes in that the earlier studies also showed the effects of compound administration on survival (Weisburger, 1977). The short-chain halogenated aliphatic hydrocarbon class of chemicals presents major problems in the selection of doses. In future studies with related chemicals, detailed metabolism and excretion experiments should be considered, with thought also given to the use of more than a control and two dosage levels in the bioassay. Such an approach would reduce the risk of generating equivocal data.

The major lesion produced in rats by the administration of pentachloroethane was a chronic, diffuse inflammation of the kidneys in males (control, 4/50, 8%; low-dose, 14/49, 29%; high-dose, 33/50, 66%). This lesion was distinguishable from the nephropathy normally seen in aging F344/N rats, and some of the dosed males had both types of change. The occurrence of this nonneoplastic effect in females was 0/44, 0/47, and 4/45. Mineralization of the renal papilla in dosed males was considered to be secondary to the lesion induced by compound administration rather than a direct effect. [See on page 8 Note Added Subsequent to Peer Review.]

Interstitial-cell tumors of the testis in male rats showed an increasing trend ($P < 0.05$) by the life table test, but a decreasing trend ($P < 0.05$) by the Cochran-Armitage test (Table 5). Since most F344/N male rats eventually develop these tumors, the life table analysis reflects primarily the significantly reduced overall survival observed in high-dose male rats. In contrast, the Cochran-Armitage test reflects the decreased tumor incidence observed in the dosed groups. Since this lesion is not generally regarded as fatal and the Cochran-Armitage test ignores survival differences, the most meaningful analysis is the incidental tumor test, which indicates no significant ($P > 0.1$) effect due to the administration of pentachloroethane.

Although the survival of the dosed mice was compromised by the dosage levels employed, the hepatocarcinogenicity of pentachloroethane was clearly established. The times to the first and second hepatocellular carcinomas in the high-dose male group were only 35 and 39 weeks, respectively. By week 41, when the 8 surviving high-dose males were killed, 7/45 (16%) of the animals in this group had the lesion. None of the 25 control males sacrificed at 44 weeks were found to have hepatocellular carcinoma. This difference in tumor incidence was dose related ($P < 0.001$), and the incidence was increased in the low-dose ($P < 0.001$) and high-dose ($P < 0.049$) groups compared with concurrent controls. Early mortality of high-dose mice precluded an evaluation of their lifetime incidence of hepatocellular tumors. The conclusion of hepatocarcinogenicity in mice is strengthened by the significantly ($P < 0.001$) increased incidences of hepatocellular carcinoma in the low-dose male group and in both dosed groups of females. Furthermore, female mice had significantly ($P < 0.001$) elevated incidences of hepatocellular adenomas.

The early killing of 25 male control mice did not affect the overall incidence of hepatocellular carcinoma in the control group relative to past control experience. Table 11 summarizes the incidences of both hepatocellular adenomas and carcinomas among animals in the present study, previous control groups from the same laboratory, and historical controls from all laboratories. Although the male control incidence of adenomas in the present study was somewhat higher than in previous control groups, the incidences of hepatocellular carcinoma among the control groups from the present study were similar to those of historical controls. Further, the incidence of hepatocellular carcinoma observed in the low-dose males and both groups of dosed females far exceeded the historical control rates of this tumor, despite the reduced survival. The absence of a dose-related increase for the incidences of hepatocellular carcinoma in either males or females is likely to be a reflection of the shorter survival times of the high-dose animals.

TABLE 11. INCIDENCE OF LIVER TUMORS IN MICE IN THE PRESENT STUDY AND IN VEHICLE CONTROL GROUPS IN NCI/NTP BIOASSAYS OF 104 WEEKS

Tumor Type	Pentachloroethane			Same Laboratory			Incidence at All Laboratories in Bioassay Program
	Vehicle Control	Low Dose	High Dose	Incidence	Range Low	Range High	
Adenoma							
Male	5/23 (22%) *(a)*	4/44 (9%)	7/45 (16%) *(b)*	33/240 (14%)	8%	21%	99/904 (11.0%)
Female	2/46 (4%)	8/42 (19%)	19/45 (42%) *(c)*	15/334 (4%)	3%	8%	38/996 (3.8%)
Carcinoma							
Male	4/23 (17%) *(a)*	26/44 (59%)	7/45 (16%) *(b)*	48/240 (20%)	8%	32%	187/904 (20.7%)
Female	1/46 (2%)	28/42 (67%)	13/45 (29%) *(c)*	11/334 (3%)	0%	6%	30/996 (3.0%)
Adenoma or Carcinoma							
Male	9/23 (39%) *(a)*	30/44 (68%)	14/45 (31%) *(b)*	80/240 (33%)	25%	42%	276/904 (30.5%)
Female	3/46 (7%)	36/42 (86%)	32/45 (71%) *(c)*	26/334 (8%)	4%	10%	67/996 (6.7%)

(a) Does not include 25 male mice killed during week 44. When these animals are included, the incidences are: adenoma 10/48 (21%), carcinoma 4/48 (8%), adenoma or carcinoma 14/48 (29%).

(b) All males were dead by week 41.

(c) All females were dead by week 74.

Life table analysis indicated a significant ($P < 0.05$) positive trend for lung adenomas and pituitary adenomas in female mice. However, since it was unlikely that these tumors were the cause of death and the alternative analyses revealed little evidence of an effect, these changes were not attributed to the administration of pentachloroethane.

Pentachloroethane has been reported to be metabolized to trichloroethylene (2% to 16% of the dose) and tetrachloroethylene (3% to 9% of the dose) in NMRI mice (Yllner, 1971). Both of these chloroethylenes have been shown to cause hepatocellular carcinoma in B6C3F$_1$ mice, but not in Osborne-Mendel rats (NCI, 1977; 1976).* If a similar metabolic pattern is assumed between NMRI and B6C3F$_1$ mice, the low- and high-dose animals in the present study could have been indirectly exposed to 40-80 and 23-46 mg/kg/day of trichloroethylene and tetrachloroethylene, respectively. Therefore, it is possible that the carcinogenic action of pentachloroethane in mice is mediated through the biotransformation of the parent chemical to these active chloroethylenes. However, sufficient data do not exist to allow an adequate assessment of this possibility. The lowest doses of trichloroethylene (1,169 mg/kg/day in males and 869 mg/kg/day in females) and tetrachloroethylene (536 mg/kg/day in males and 386 mg/kg/day in females) tested earlier were associated with a high incidence of hepatocellular carcinoma. Further, these treatments with the chloroethylenes reduced the survival of test animals, an effect that could result in an underestimation of carcinogenic potency.

Hexachloroethane, the major contaminant (4.2%) in the pentachloroethane sample used for the chronic study, has also been shown to induce hepatocellular carcinoma in mice but not rats (NCI, 1978a). The low- and high-dose mice in the present study were exposed to doses of hexachloroethane of 10.5 and 21 mg/kg/day, respectively. In the earlier study, the lowest dose of

*Although in the earlier study on trichloroethylene (NCI, 1977) small amounts of epichlorohydrin (0.09%) and 1,2-epoxybutane (0.19%) were present in the test material, a more recent study (NTP 1983) has confirmed the hepatocarcinogenicity of epichlorohydrin-free trichloroethylene in male and female B6C3F$_1$ mice.

hexachloroethane (590 mg/kg/day) produced significant increases in hepatocellular carcinoma in both sexes of mice. Although it is impossible to assess adequately the potential impact of this contaminant on the outcome of the present study, it seems unlikely that the relatively low dose of hexachloroethane could have produced the high incidence of hepatocellular carcinoma seen in this study. However, an additive or potentiating interaction between pentachloroethane and hexachloroethane and the chloroethylene metabolites of the parent compound cannot be dismissed as a potential mechanism of carcinogenesis.

Weisburger (1977) summarized the results of a series of carcinogenesis bioassays of chlorohydrocarbons. The similarities between the effects of pentachloroethane and the previously tested chloroethylenes, chloroethanes, carbon tetrachloride, and chloroform are striking. In general, each of these chemicals induced a high incidence of hepatocellular carcinoma in mice, and had little or no carcinogenic effect in Osborne-Mendel rats. The same or similar mechanisms of action, as yet to be defined, seem likely for these agents.

The NTP mutagenicity test results were negative for *S. typhimurium* (TA 98, 100, 1535, 1537) with and without exogenous metabolic activation (NTP unpublished results). Mutagenicity testing of chlorohydrocarbons using *Salmonella typhimurium* tester strains generally yields negative results (Weisburger and Williams, 1980). This observation has lead Weisburger and Williams (1978) to suggest that the induction of hepatocellular carcinoma in mice by the chlorohydrocarbons may be mediated through a promoting action. The nature of the initiator remains to be elucidated, but it could be a genetically-mediated susceptibility. This is a possible hypothesis when one considers that the control incidence of hepatocellular carcinoma is greater in B6C3F$_1$ mice (187/904, 20.7% in males and 30/996, 3.0% in females) than it is in either Osborne-Mendel (0/270 in males and 1/270, 0.37% in females) or F344/N (7/992, 0.7% in males; 1/946, 0.1% in females) rats.

The results of this study show that pentachloroethane, like other chlorohydrocarbons tested earlier, induces hepatocellular carcinoma in both male and female B6C3F$_1$ mice. While the absence of a similar effect in F344/N rats appears to be due to a species difference in sensitivity, the decreased survival of treated rats must also be considered as a possible cause for the absence of a carcinogenic effect in this species.

Conclusions: Under the conditions of this bioassay, technical grade pentachloroethane containing 4.2% hexachloroethane (a known carcinogen in mice) was not carcinogenic in F344/N rats. The decreased survival of dosed rats might have reduced the sensitivity for a carcinogenic response in this species. Pentachloroethane was nephrotoxic to male rats. Technical grade pentachloroethane was carcinogenic for B6C3F$_1$ mice, causing hepatocellular carcinomas in males and females, and adenomas in females.

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V. REFERENCES

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(50)
KERATOACANTHOMA	1 (2%)		
SARCOMA, NOS	1 (2%)		
FIBROMA	5 (10%)		
FIBROSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)	2 (4%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		1 (2%)
LEUKEMIA,NOS	2 (4%)	1 (2%)	2 (4%)
LYMPHOCYTIC LEUKEMIA		1 (2%)	1 (2%)
#SPLEEN	(50)	(48)	(50)
SARCOMA, NOS		1 (2%)	
#LYMPH NODE	(46)	(40)	(46)
MALIGNANT LYMPHOMA, NOS			1 (2%)
#LIVER	(50)	(48)	(50)
LEUKEMIA,NOS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
*SKIN	(50)	(49)	(50)
HEMANGIOPERICYTOMA, NOS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(47)	(49)
FIBROSARCOMA			1 (2%)
#LIVER	(50)	(48)	(50)
BILE DUCT CARCINOMA			1 (2%)
NEOPLASTIC NODULE		1 (2%)	1 (2%)
HEPATOCELLULAR CARCINOMA	2 (4%)		
#HEPATIC CAPSULE	(50)	(48)	(50)
MESOTHELIOMA, NOS	1 (2%)		
#STOMACH	(46)	(43)	(42)
PAPILLOMATOSIS		1 (2%)	
SQUAMOUS CELL CARCINOMA	1 (2%)		
URINARY SYSTEM			
†#KIDNEY	(50)	(49)	(50)
CARCINOMA,NOS		1 (2%)	
TUBULAR-CELL ADENOMA		1 (2%)	4 (8%)
TUBULAR-CELL ADENOCARCINOMA	1 (2%)	1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(46)	(46)
ADENOMA, NOS	3 (6%)	3 (7%)	1 (2%)
CHROMOPHOBE ADENOMA	20 (42%)	10 (22%)	3 (7%)
#ADRENAL	(49)	(48)	(50)
ADENOMA, NOS		1 (2%)	
PHEOCHROMOCYTOMA	3 (6%)	1 (2%)	4 (8%)
#THYROID	(50)	(45)	(46)
ADENOMA, NOS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
† SEE PAGE 8, NOTE ADDED SUBSEQUENT TO PEER REVIEW

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR-CELL CARCINOMA	1 (2%)		
C-CELL ADENOMA	6 (12%)	6 (13%)	3 (7%)
#PANCREATIC ISLETS	(48)	(48)	(50)
ISLET-CELL ADENOMA	4 (8%)	5 (10%)	
ISLET-CELL CARCINOMA	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(50)
FIBROMA	2 (4%)	1 (2%)	
LIPOMA		1 (2%)	
FIBROADENOMA	1 (2%)	1 (2%)	
*PREPUTIAL GLAND	(50)	(49)	(50)
ADENOCARCINOMA, NOS		1 (2%)	
#TESTIS	(49)	(47)	(49)
INTERSTITIAL-CELL TUMOR	41 (84%)	34 (72%)	33 (67%)
SEMINOMA/DYSGERMINOMA	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(50)	(47)	(49)
GLIOMA, NOS	1 (2%)		
#MEDULLA OBLONGATA	(50)	(47)	(49)
NEUROMA	1 (2%)		
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(49)	(50)
CARCINOMA,NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(49)	(50)
LIPOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MESOTHELIOMA, NOS			2 (4%)
*PERITONEUM	(50)	(49)	(50)
MESOTHELIOMA, NOS	1 (2%)	1 (2%)	
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	6	15	16
MORIBUND SACRIFICE	3	2	7
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	41	33	26
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			1
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	48	39	36
TOTAL PRIMARY TUMORS	106	77	62
TOTAL ANIMALS WITH BENIGN TUMORS	46	38	36
TOTAL BENIGN TUMORS	88	67	50
TOTAL ANIMALS WITH MALIGNANT TUMORS	11	8	5
TOTAL MALIGNANT TUMORS	16	8	8
TOTAL ANIMALS WITH SECONDARY TUMORS#			
TOTAL SECONDARY TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	4
TOTAL UNCERTAIN TUMORS	2	2	4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	49	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	48
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(49)	(48)
FIBROMA	1 (2%)		
FIBROSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(49)	(48)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
BILE DUCT CARCINOMA, METASTATIC	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(49)	(48)
MALIGNANT LYMPHOMA, NOS	1 (2%)	3 (6%)	1 (2%)
LEUKEMIA,NOS		3 (6%)	1 (2%)
LYMPHOCYTIC LEUKEMIA			1 (2%)
#LIVER	(49)	(48)	(45)
LYMPHOCYTIC LEUKEMIA	1 (2%)	1 (2%)	
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
#LIVER	(49)	(48)	(45)
BILE DUCT CARCINOMA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NEOPLASTIC NODULE		2 (4%)	
HEPATOCELLULAR CARCINOMA	1 (2%)	1 (2%)	
URINARY SYSTEM			
#KIDNEY	(44)	(47)	(45)
LIPOMA		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(46)	(45)
ADENOMA, NOS	3 (6%)	3 (7%)	
CHROMOPHOBE ADENOMA	23 (47%)	14 (30%)	12 (27%)
BASOPHIL ADENOMA	1 (2%)		
#ADRENAL	(48)	(49)	(46)
ADENOMA, NOS	1 (2%)		
PHEOCHROMOCYTOMA	2 (4%)	1 (2%)	
#ADRENAL MEDULLA	(48)	(49)	(46)
GANGLIONEUROMA	1 (2%)		
#THYROID	(46)	(48)	(45)
FOLLICULAR-CELL ADENOMA			1 (2%)
FOLLICULAR-CELL CARCINOMA			1 (2%)
C-CELL ADENOMA	4 (9%)	3 (6%)	2 (4%)
PAPILLARY CYSTADENOMA, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(49)	(48)
ADENOCARCINOMA, NOS	2 (4%)	1 (2%)	1 (2%)
FIBROMA		2 (4%)	
FIBROADENOMA	9 (18%)	8 (16%)	10 (21%)
*CLITORAL GLAND	(49)	(49)	(48)
ADENOCARCINOMA, NOS	1 (2%)		
#UTERUS	(45)	(48)	(40)
ADENOMA, NOS			1 (3%)
ADENOCARCINOMA, NOS		2 (4%)	
FIBROSARCOMA			1 (3%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOMETRIAL STROMAL POLYP	7 (16%)	12 (25%)	2 (5%)
ENDOMETRIAL STROMAL SARCOMA	2 (4%)		
#OVARY	(47)	(48)	(45)
CYSTADENOMA, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(42)	(46)	(46)
GLIOMA, INVASIVE		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(49)	(49)	(48)
FIBROSARCOMA			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(49)	(48)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
BILE DUCT CARCINOMA, INVASIVE	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	6	21
MORIBUND SACRIFICE	5	7	2
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED		1	2
TERMINAL SACRIFICE	38	36	25
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	37	36	26
TOTAL PRIMARY TUMORS	63	59	36
TOTAL ANIMALS WITH BENIGN TUMORS	33	30	21
TOTAL BENIGN TUMORS	53	45	29
TOTAL ANIMALS WITH MALIGNANT TUMORS	9	9	5
TOTAL MALIGNANT TUMORS	10	12	7
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	2	1
TOTAL SECONDARY TUMORS	2	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT		2	
TOTAL UNCERTAIN TUMORS		2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	102	101	104	104	104	104	104	104	103	093	104	104	104	104	103	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KERATOACANTHOMA																			X						
SARCOMA, NOS																X	X								
FIBROMA			X														X				X				
FIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
ALVEOLAR/BRONCHIOLAR ADENOMA						X																			
ALVEOLAR/BRONCHIOLAR CARCINOMA																						X			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+
THYMUS	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA										X									X						
MESOTHELIOMA, NOS																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																									
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS						X									X								X		
CHROMOPHOBE ADENOMA	X	X	X				X		X			X	X	X										X	
ADRENAL	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																						X			
C-CELL ADENOMA												X											X		
PARATHYROID	-	+	-	+	+	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA						X										X				X					
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	+	+	+	N	+	N	N
FIBROMA											X														
FIBROADENOMA											X														
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X		X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X		X	X
SEMINOMA/DYSGERMINOMA			X																						
PROSTATE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, NOS															X										
NEUROMA																									
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS									X																
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS										X															
LEUKEMIA,NOS										X															

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	099	104	104	104	104	100	104	104	104	100	104	104	104	104	104	104	104	104	091	104		
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																									X	1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
KERATOACANTHOMA														X												1
SARCOMA, NOS																										1
FIBROMA							X																			5
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																									X	1
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	46
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	2
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA																										2
MESOTHELIOMA, NOS																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
SQUAMOUS CELL CARCINOMA													X													1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOCARCINOMA		X																								1
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																										3
CHROMOPHOBE ADENOMA	X	X	X	X	X	X					X		X		X			X						X		20
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA		X		X											X											3
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL CARCINOMA																										1
C-CELL ADENOMA			X			X														X			X			6
PARATHYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	-	+	+	-	+	-	39
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL ADENOMA			X																							4
ISLET-CELL CARCINOMA		X																								1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	+	N	N	N	+	N	N	N	N	N	N	N	N	N	+	N	N	+	N	50
FIBROMA																							X			2
FIBROADENOMA																										1
TESTIS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR		X	X		X	X	X	X				X	X		X	X	X	X	X	X	X	X	X	X	41
SEMINOMA/DYSGERMINOMA																										1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	47
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GLIOMA, NOS										X																1
NEUROMA																										1
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MESOTHELIOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MALIGNANT LYMPHOMA, NOS																										1
LEUKEMIA, NOS							X																			2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	018	018	104	088	041	017	041	103	104	086	041	072	361	041	104	104	041	041	041	041	041	041	041	104	103
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA														X											
TRACHEA	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	-	+	+	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
LYMPH NODES	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+
THYMUS	+	-	-	-	-	+	-	-	-	A	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE								X							X										
LEUKEMIA,NOS																									
BILE DUCT	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
STOMACH	-	+	+	-	+	+	+	-	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMATOSIS							X																		
SMALL INTESTINE	-	+	+	-	+	+	+	-	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
LARGE INTESTINE	-	-	+	-	+	+	+	-	+	A	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
TUBULAR-CELL ADENOMA																									
TUBULAR-CELL ADENOCARCINOMA								X																	
URINARY BLADDER	+	+	-	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X																		X				
CHROMOPHOBE ADENOMA				X			X												X		X		X		X
ADRENAL	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
PHEOCHROMOCYTOMA			X																						
THYROID	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA								X														X			
PARATHYROID	+	-	-	+	-	+	+	-	-	A	+	+	-	+	+	-	+	+	+	-	-	+	+	-	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA							X							X											X
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	+	N	N	N	N	A	N	N	+	N	N	N	+	+	N	N	N	+	N	+	N
FIBROMA					X																				
LIPOMA																									
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
INTERSTITIAL-CELL TUMOR			X		X			X	X		X			X	X	X	X	X	X	X	X			X	
PROSTATE	+	+	-	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	-	+	+	+	-
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS																									
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																				X					
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS																									
LYMPHOCYTIC LEUKEMIA																									X

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	02606	02617	02809	02901	03011	03112	03311	03404	03505	03601	03704	03807	03904	04011	04104	04218	04304	04411	04504	04617	04804	04904	05010	TOTAL
WEEKS ON STUDY	030	004	004	004	004	004	004	004	019	004	004	861	004	017	081	004	004	004	059	004	073	004	004	TISSUES TUMORS
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA	X																							2
TRACHEA	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS																X								1
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	+	-	-	+	+	-	+	40
THYMUS	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	5
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NEOPLASTIC NODULE																								1
LEUKEMIA,NOS																								1
BILE DUCT	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	45
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	43
PAPILLOMATOSIS																								1
SMALL INTESTINE	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	40
LARGE INTESTINE	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	38
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS				X																				1
TUBULAR-CELL ADENOMA																				X				1
TUBULAR-CELL ADENOCARCINOMA																								1
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	44
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	-	+	+	+	+	+	46
ADENOMA, NOS													X											3
CHROMOPHOBE ADENOMA		X							X							X						X		10
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48
ADENOMA, NOS									X															1
PHEOCHROMOCYTOMA																								1
THYROID	-	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	45
C-CELL ADENOMA		X		X												X	X							6
PARATHYROID	-	+	-	+	-	-	-	+	-	-	-	+	+	+	+	+	+	-	-	+	+	-	+	27
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL ADENOMA								X	X															5
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	+	N	N	+	+	N	+	N	N	N	N	N	+	N	N	+	N	N	N	N	N	+	N	N	49*
FIBROMA																								1
LIPOMA				X																				1
FIBROADENOMA							X																	1
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
INTERSTITIAL-CELL TUMOR		X	X	X		X	X	X	X		X	X	X	X		X	X	X	X		X	X		X	X	34
PROSTATE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	43
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
ADENOCARCINOMA, NOS		X																						1
NERVOUS SYSTEM																								
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPECIAL SENSE ORGANS																								
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	49*
CARCINOMA,NOS																						X		1
BODY CAVITIES																								
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
MESOTHELIOMA, NOS																								1
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
LEUKEMIA,NOS												X												1
LYMPHOCYTIC LEUKEMIA																								1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	093	104	104	091	055	104	104	104	104	104	104	104	104	104	066	018	104	041	072	104	105	104	104	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOPERICYTOMA, NOS								X																	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
THYMUS	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																									
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT CARCINOMA																									
NEOPLASTIC NODULE														X											
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-
SMALL INTESTINE	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	-
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA			X																	X					
URINARY BLADDER	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																				X					
CHROMOPHOBE ADENOMA									X																
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA						X										X									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+
ADENOMA, NOS											X														
C-CELL ADENOMA			X	X																					
PARATHYROID	-	+	+	-	+	+	+	+	-	+	+	-	-	-	+	-	+	+	-	-	-	-	-	+	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																								X	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	+	N	N	N	N	+	N	N	N	N	+	+	N	N	N	N	N	N	N	N	N	N
TESTIS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR			X	X		X	X	X		X	X	X	X	X			X	X	X	X		X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LIPOMA																									
MESOTHELIOMA, NOS																								X	
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																									
LEUKEMIA,NOS							X																		
LYMPHOCYTIC LEUKEMIA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	032	091	118	118	012	097	079	033	054	041	041	044	044	036	010	012	092	014	044	075	036	099	041	041	048	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
HEMANGIOPERICYTOMA, NOS																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	46
MALIGNANT LYMPHOMA, NOS						X																				1
THYMUS	-	-	+	-	-	-	-	+	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	6
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
FIBROSARCOMA																			X							1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT CARCINOMA						X																				1
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	45
STOMACH	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	-	42
SMALL INTESTINE	+	-	+	+	+	+	+	+	-	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	-	39
LARGE INTESTINE	+	-	+	+	-	+	+	+	-	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	-	38
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOMA		X															X									4
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	46
ADENOMA, NOS																										1
CHROMOPHOBE ADENOMA						X					X															3
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA					X												X									4
THYROID	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS																										1
C-CELL ADENOMA										X																3
PARATHYROID	+	+	-	+	-	+	-	-	-	+	+	+	+	-	-	+	+	+	+	+	-	+	+	+	+	30
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL CARCINOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	N	N	N	+	N	+	N	N	N	N	N	+	N	N	N	N	N	+	+	N	N	+	N	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR		X			X	X				X	X	X	X				X	X	X	X			X	X	X	33
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	47
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
LIPOMA										X																1
MESOTHELIOMA, NOS						X																				2
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS																									X	1
LEUKEMIA,NOS						X																				2
LYMPHOCYTIC LEUKEMIA																									X	1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	101	104	104	104	104	104	104	093	104	104	104	104	104	104	104	104	089	104	104	094	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT CARCINOMA, METASTATIC																						X			
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	-	+	+	+	-	+	+	+	-
SPLEEN	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+
THYMUS	-	-	+	-	-	-	-	+	+	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT CARCINOMA																						X			
HEPATOCELLULAR CARCINOMA																									
LYMPHOCYTIC LEUKEMIA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	-	+	+	+	+	+	A	+	+	-	+	+	+	-	+	+	+	-	+	-	+	+
URINARY BLADDER	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X				X	X				X	X		X			X	X	X	X	X		X		X
CHROMOPHOBE ADENOMA																									
BASOPHIL ADENOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ADENOMA, NOS												X	X		X										
PHEOCHROMOCYTOMA																									
GANGLIONEUROMA																									
THYROID	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+
C-CELL ADENOMA																							X		
PAPILLARY CYSTADENOMA, NOS	X																								X
PARATHYROID	-	+	-	-	+	-	-	-	-	A	-	+	+	+	-	-	+	-	+	+	-	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	N	+	A	+	+	+	+	+	+	N	+	+	N	+	+	N	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA			X														X				X				
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS																					X				
UTERUS	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP		X				X						X													X
ENDOMETRIAL STROMAL SARCOMA																							X		
OVARY	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BILE DUCT CARCINOMA, INVASIVE																						X			
MALIGNANT LYMPHOMA, NOS			X																						

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL
WEEKS ON STUDY	104	104	069	104	104	104	067	104	101	080	104	102	104	093	104	104	104	067	104	093	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	49*
FIBROMA																		X								1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
BILE DUCT CARCINOMA, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR CARCINOMA		X																								1
TRACHEA	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	42
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+	-	+	+	+	42
THYMUS	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
BILE DUCT CARCINOMA																										1
HEPATOCELLULAR CARCINOMA						X																				1
LYMPHOCYTIC LEUKEMIA	X																									1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	+	N	+	N	N	N	N	N	N	N	N	N	N	N	N	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	-	+	+	-	+	+	-	+	+	+	+	+	-	+	+	-	+	+	-	+	+	+	-	+	+	39
STOMACH	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS														X					X			X				3
CHROMOPHOBE ADENOMA		X	X		X			X	X	X		X					X			X					X	23
BASOPHIL ADENOMA																		X								1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																										1
PHEOCHROMOCYTOMA																										2
GANGLIONEUROMA				X																						1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-CELL ADENOMA										X													X			4
PAPILLARY CYSTADENOMA, NOS																										1
PARATHYROID	+	-	+	+	-	-	-	+	+	-	-	+	-	-	-	-	-	+	-	-	+	-	-	+	+	22
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	49*
ADENOCARCINOMA, NOS										X		X						X		X		X			X	2
FIBROADENOMA								X													X		X			9
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
ADENOCARCINOMA, NOS																										1
UTERUS	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	45
ENDOMETRIAL STROMAL POLYP				X	X				X																	7
ENDOMETRIAL STROMAL SARCOMA	X																									2
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
BILE DUCT CARCINOMA, INVASIVE																										1
MALIGNANT LYMPHOMA, NOS																										1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	104	104	081	104	104	104	104	104	102	104	104	070	104	104	091	104	104	102	104	097	061	092	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	A	+	+
FIBROSARCOMA							X																		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
TRACHEA	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	A	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	A	+	+	
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	A	+	+	
LYMPH NODES	+	-	+	+	+	-	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	A	+	+	
THYMUS	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	A	-	-	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	A	+	+	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	
NEOPLASTIC NODULE										X															
HEPATOCELLULAR CARCINOMA																									
LYMPHOCYTIC LEUKEMIA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	A	+	+	
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	A	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	+	A	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	A	+	+
LIPOMA							X																		
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	A	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	A	+	+
ADENOMA, NOS								X				X	X												
CHROMOPHOBE ADENOMA										X							X	X						X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
PHEOCHROMOCYTOMA															X										
THYROID	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
C-CELL ADENOMA	X						X																		
PARATHYROID	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	+	+	N	+	N	N	N	+	+	N	+	N	+	N	+	+	+	N	A	+	N
ADENOCARCINOMA, NOS																									
FIBROMA																									
FIBROADENOMA				X																					
UTERUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
ADENOCARCINOMA, NOS																				X					
ENDOMETRIAL STROMAL POLYP							X										X	X				X			
OVARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
CYSTADENOMA, NOS											X														
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
GLIOMA, INVASIVE																	X								
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N
ADENOCARCINOMA, NOS, METASTATIC																				X					
MALIGNANT LYMPHOMA, NOS			X																						
LEUKEMIA,NOS			X		X					X															

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	07761	07778	07790	08081	08122	08183	08244	08255	08266	08287	08298	08904	09011	09122	09134	09145	09156	09167	09178	09189	09190	TOTAL TISSUES TUMORS
WEEKS ON STUDY	091	104	104	103	091	104	080	104	104	104	099	104	104	104	104	104	104	104	102	104	104	
INTEGUMENTARY SYSTEM																						
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49M
FIBROSARCOMA																						1
RESPIRATORY SYSTEM																						
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																						
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	46
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	41
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2
CIRCULATORY SYSTEM																						
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																						
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	48
NEOPLASTIC NODULE																X						2
HEPATOCELLULAR CARCINOMA																		X				1
LYMPHOCYTIC LEUKEMIA										X												1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	48
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	44
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	45
URINARY SYSTEM																						
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	47
LIPOMA																						1
URINARY BLADDER	+	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	41
ENDOCRINE SYSTEM																						
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS																						3
CHROMOPHOBE ADENOMA	X				X	X	X	X	X									X		X	X	14
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA																						1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-CELL ADENOMA					X																	3
PARATHYROID	+	-	+	+	+	-	+	-	-	+	-	-	-	-	+	+	-	+	+	+	-	37
REPRODUCTIVE SYSTEM																						
MAMMARY GLAND	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	49M
ADENOCARCINOMA, NOS				X																		1
FIBROMA														X						X		2
FIBROADENOMA	X					X	X	X		X					X				X			8
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOCARCINOMA, NOS																		+				2
ENDOMETRIAL STROMAL POLYP				X						X	X			X	X	X			X	X		12
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CYSTADENOMA, NOS																						1
NERVOUS SYSTEM																						
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	46
GLIOMA, INVASIVE																						1
ALL OTHER SYSTEMS																						
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M
ADENOCARCINOMA, NOS, METASTATIC																						1
MALIGNANT LYMPHOMA, NOS												X							X			3
LEUKEMIA,NOS																						3

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	101	004	004	038	033	004	004	041	054	041	011	041	098	049	090	049	110	041	041	020	067	041	041	041	090
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	A	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																									
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
SPLEEN	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	A	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	-
THYMUS	-	-	-	+	A	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+
BILE DUCT	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	-	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+
STOMACH	-	+	+	+	A	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	-	+	+	+	A	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	-	+	+	-	A	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	+	+	+	A	+	+	-	+	-	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+
CHROMOPHOBE ADENOMA	X		X				X			X	X		X				X		X						X
ADRENAL	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																	X								
FOLLICULAR-CELL CARCINOMA																									
C-CELL ADENOMA										X															
PARATHYROID	+	+	+	-	A	+	-	-	-	-	-	-	+	+	+	+	-	+	-	+	-	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	N	A	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	N	+	+	+
ADENOCARCINOMA, NOS								X																	
FIBROADENOMA	X	X	X				X									X		X						X	
UTERUS	-	+	+	+	A	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
ADENOMA, NOS										X															
FIBROSARCOMA																					X				
ENDOMETRIAL STROMAL POLYP																									
OVARY	-	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
MESENTERY	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA																					X				
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS															X										
LEUKEMIA,NOS																									
LYMPHOCYTIC LEUKEMIA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	07761	07778	07901	08011	08212	08334	08545	08561	08781	08890	09011	09123	09341	09521	09667	09788	09901	10017	TOTAL
WEEKS ON STUDY	09041	10417	07178	10404	03505	09416	01650	04061	10041	05040	04041	04041	04041	04041	04041	04111	04041	04041	TISSUES / TUMORS
RESPIRATORY SYSTEM																			
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	48
ADENOCARCINOMA, NOS, METASTATIC																			1
ALVEOLAR/BRONCHIOLAR ADENOMA			X																1
TRACHEA	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	-	+	+	46
HEMATOPOIETIC SYSTEM																			
BONE MARROW	-	+	+	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	44
SPLEEN	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	-	+	+	45
LYMPH NODES	+	+	+	+	+	+	+	A	+	-	+	+	-	+	+	+	+	+	41
THYMUS	-	-	-	-	-	+	-	A	+	+	-	-	+	-	-	-	-	-	8
CIRCULATORY SYSTEM																			
HEART	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																			
SALIVARY GLAND	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	46
LIVER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	45
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	45
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	48
PANCREAS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	46
ESOPHAGUS	+	+	+	+	+	+	-	A	+	+	+	+	+	+	-	+	+	+	42
STOMACH	+	+	+	+	+	+	-	A	-	+	+	+	-	+	+	+	-	+	39
SMALL INTESTINE	+	+	+	+	+	+	+	A	-	+	+	+	-	+	+	-	+	-	38
LARGE INTESTINE	+	+	+	+	+	+	+	A	-	+	+	+	-	+	+	-	+	-	38
URINARY SYSTEM																			
KIDNEY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	-	45
URINARY BLADDER	+	+	+	+	-	+	-	A	+	+	+	+	+	+	+	-	+	-	37
ENDOCRINE SYSTEM																			
PITUITARY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	45
CHROMOPHOBE ADENOMA																X	X	X	12
ADRENAL	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	-	+	46
THYROID	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	-	+	+	45
FOLLICULAR-CELL ADENOMA																			1
FOLLICULAR-CELL CARCINOMA												X							1
C-CELL ADENOMA		X																	2
PARATHYROID	-	+	+	-	-	+	-	A	+	-	+	-	+	+	+	+	-	+	28
REPRODUCTIVE SYSTEM																			
MAMMARY GLAND	+	+	N	+	+	+	N	A	N	N	+	+	N	+	+	+	N	+	48
ADENOCARCINOMA, NOS																			1
FIBROADENOMA	X		X													X			10
UTERUS	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	-	+	40
ADENOMA, NOS																			1
FIBROSARCOMA																			1
ENDOMETRIAL STROMAL POLYP		X											X						2
OVARY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	-	+	45
BODY CAVITIES																			
MESENTERY	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	48
FIBROSARCOMA																			1
ALL OTHER SYSTEMS																			
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	48
MALIGNANT LYMPHOMA, NOS							X												1
LEUKEMIA,NOS																			1
LYMPHOCYTIC LEUKEMIA							X												1

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	44	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	44	45
INTEGUMENTARY SYSTEM			
*MULTIPLE ORGANS	(48)	(44)	(45)
FIBROUS HISTIOCYTOMA, MALIGNANT		1 (2%)	
*SUBCUT TISSUE	(48)	(44)	(45)
FIBROMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(47)	(41)	(44)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)	2 (5%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (6%)	4 (10%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA	3 (6%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(44)	(45)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#SPLEEN	(46)	(38)	(42)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
CIRCULATORY SYSTEM			
#SPLEEN	(46)	(38)	(42)
HEMANGIOMA	3 (7%)	2 (5%)	
#LIVER	(48)	(44)	(45)
HEMANGIOMA	1 (2%)	3 (7%)	
HEMANGIOSARCOMA		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#LIVER	(48)	(44)	(45)
HEPATOCELLULAR ADENOMA	10 (21%)	4 (9%)	7 (16%)
HEPATOCELLULAR CARCINOMA	4 (8%)	26 (59%)	7 (16%)
#STOMACH	(46)	(37)	(40)
SQUAMOUS CELL PAPILLOMA		3 (8%)	
BASAL-CELL CARCINOMA		1 (3%)	
#JEJUNUM	(45)	(30)	(37)
PAPILLARY ADENOMA		1 (3%)	
URINARY SYSTEM			
#KIDNEY	(47)	(40)	(45)
TUBULAR-CELL ADENOCARCINOMA	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(35)	(25)	(34)
ADENOMA, NOS			1 (3%)
#ADRENAL	(47)	(40)	(45)
PHEOCHROMOCYTOMA	1 (2%)		
#THYROID	(45)	(37)	(36)
FOLLICULAR-CELL ADENOMA	1 (2%)	1 (3%)	
REPRODUCTIVE SYSTEM			
NONE			
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(48)	(44)	(45)
SARCOMA, NOS	1 (2%)	2 (5%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	21	19
MORIBUND SACRIFICE	1	7	23
SCHEDULED SACRIFICE	25		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	19	22	8
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	20	38	14
TOTAL PRIMARY TUMORS	29	52	15
TOTAL ANIMALS WITH BENIGN TUMORS	15	15	7
TOTAL BENIGN TUMORS	19	19	8
TOTAL ANIMALS WITH MALIGNANT TUMORS	7	31	7
TOTAL MALIGNANT TUMORS	10	33	7
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	2	
TOTAL SECONDARY TUMORS	1	2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	43	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	43	45
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#LUNG	(46)	(41)	(41)
CARCINOMA, NOS, METASTATIC	1 (2%)		
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (7%)		3 (7%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
OSTEOSARCOMA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(43)	(45)
MALIGNANT LYMPHOMA, NOS	7 (15%)	2 (5%)	1 (2%)
#SPLEEN	(45)	(35)	(41)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#LIVER	(46)	(42)	(45)
MALIGNANT LYMPHOMA, NOS			1 (2%)
#JEJUNUM	(39)	(21)	(22)
MALIGNANT LYMPHOMA, NOS	1 (3%)		
#KIDNEY	(42)	(39)	(43)
MALIGNANT LYMPHOMA, NOS			1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(45)	(35)	(41)
HEMANGIOSARCOMA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#LIVER	(46)	(42)	(45)
HEMANGIOMA		1 (2%)	
HEMANGIOSARCOMA	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(46)	(42)	(45)
HEPATOCELLULAR ADENOMA	2 (4%)	8 (19%)	19 (42%)
HEPATOCELLULAR CARCINOMA	1 (2%)	28 (67%)	13 (29%)
LIPOMA	1 (2%)	1 (2%)	
#STOMACH	(42)	(23)	(26)
PAPILLOMA, NOS			1 (4%)
SQUAMOUS CELL PAPILLOMA		1 (4%)	1 (4%)
#CECUM	(38)	(21)	(21)
LEIOMYOMA	1 (3%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(35)	(29)	(32)
ADENOMA, NOS	5 (14%)	3 (10%)	1 (3%)
#ADRENAL	(41)	(39)	(41)
CORTICAL CARCINOMA		1 (3%)	
PHEOCHROMOCYTOMA		1 (3%)	
#THYROID	(45)	(38)	(37)
FOLLICULAR-CELL ADENOMA	2 (4%)	1 (3%)	
REPRODUCTIVE SYSTEM			
#OVARY	(41)	(34)	(39)
CYSTADENOMA, NOS	1 (2%)		
NERVOUS SYSTEM			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(48)	(43)	(45)
PAPILLARY ADENOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*BONE	(48)	(43)	(45)
OSTEOSARCOMA	1 (2%)		
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
SITE UNKNOWN			
CARCINOMA,NOS	1		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	9	33	31
MORIBUND SACRIFICE	2	8	19
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED	1		
TERMINAL SACRIFICE	38	9	
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	22	38	33
TOTAL PRIMARY TUMORS	31	48	41
TOTAL ANIMALS WITH BENIGN TUMORS	13	13	22
TOTAL BENIGN TUMORS	16	16	25
TOTAL ANIMALS WITH MALIGNANT TUMORS	14	29	15
TOTAL MALIGNANT TUMORS	15	32	16
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	
TOTAL SECONDARY TUMORS	2	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	0012	0023	0034	0045	0056	0067	0078	0089	0091	0112	0123	0134	0145	0156	0167	0178	0189	0201	0212	0223	0234	0245
WEEKS ON STUDY	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049	049
RESPIRATORY SYSTEM																						
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
HEPATOCELLULAR CARCINOMA, METASTA																						
ALVEOLAR/BRONCHIOLAR ADENOMA	X		X																			
ALVEOLAR/BRONCHIOLAR CARCINOMA																						
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																						
BONE MARROW	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
HEMANGIOMA																						
MALIGNANT LYMPHOMA, NOS																						
LYMPH NODES	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+
THYMUS	+	+	-	-	-	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																						
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
DIGESTIVE SYSTEM																						
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X		X											X							X	X
HEPATOCELLULAR CARCINOMA																						
HEMANGIOMA																						
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																						
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																						
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																						
PITUITARY	+	+	-	+	-	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
PHEOCHROMOCYTOMA																						
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																						
PARATHYROID	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-
REPRODUCTIVE SYSTEM																						
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	-	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																						
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																						

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	104	084	104	104	102	098	104	048	085	104	104	104	104	104	101	104	104	104	104	104	104	104	104	104	TISSUES / TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEPATOCELLULAR CARCINOMA, METASTA	X																									1
ALVEOLAR/BRONCHIOLAR ADENOMA																			X							3
ALVEOLAR/BRONCHIOLAR CARCINOMA	X						X																X			3
TRACHEA	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	A	+	+	A	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	44
SPLEEN	+	+	-	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMANGIOMA								X						X								X				3
MALIGNANT LYMPHOMA, NOS	X																									1
LYMPH NODES	+	+	-	+	-	A	+	-	A	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	38
THYMUS	-	-	-	-	-	A	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	20
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEPATOCELLULAR ADENOMA															X					X	X		X	X		10
HEPATOCELLULAR CARCINOMA	X			X								X							X							4
HEMANGIOMA								X																		1
BILE DUCT	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	+	N	N	N	+	A	+	+	A	+	+	+	+	N	+	+	+	+	N	N	N	+	N	+	N	48*
PANCREAS	+	+	-	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	+	A	+	+	A	+	+	-	+	+	-	-	+	+	+	+	+	+	+	-	+	42
STOMACH	+	+	+	+	+	A	+	+	A	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	46
SMALL INTESTINE	+	+	-	+	+	A	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
LARGE INTESTINE	+	+	-	+	+	A	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	47
TUBULAR-CELL ADENOCARCINOMA																							X			1
URINARY BLADDER	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	43
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	-	-	A	+	+	A	-	+	+	+	+	-	+	+	-	-	-	-	+	+	+	+	35
ADRENAL	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PHEOCHROMOCYTOMA													X													1
THYROID	-	+	+	+	+	A	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA																		X								1
PARATHYROID	-	+	-	-	-	A	+	+	A	-	+	-	-	-	+	-	+	-	-	+	+	-	+	-	-	30
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
TESTIS	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
PROSTATE	+	+	-	+	+	A	+	+	A	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	41
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
SARCOMA, NOS		X																								1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	084	104	104	095	104	084	099	068	086	104	104	069	104	103	104	104	104	104	104	104	084	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE FIBROMA	+	N	+	+	+	+	+	+	A	A	+	+	+	N	+	N	+	+	N	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	-	+	+	+	+	+	+	A	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																					X				
ALVEOLAR/BRONCHIOLAR ADENOMA			X	X																					
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	-	+	+	+	A	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	A	A	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+
SPLEEN	+	+	+	+	+	+	-	+	A	A	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+
HEMANGIOMA												X													
LYMPH NODES	+	-	-	+	-	+	-	-	A	A	+	+	+	-	+	+	+	+	+	+	-	-	+	+	
THYMUS	-	-	-	-	-	-	-	-	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	A	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	-	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA		X																X							
HEPATOCELLULAR CARCINOMA	X						X	X			X	X		X		X	X		X		X	X	X	X	X
HEMANGIOMA					X																				
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	N	+	N	N	N	A	A	N	N	+	+	N	+	+	+	N	+	N	N	+	+	+
PANCREAS	+	+	+	+	+	+	-	+	A	A	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+
ESOPHAGUS	+	+	+	+	-	+	+	+	A	A	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+
STOMACH	+	-	+	+	+	+	+	+	A	A	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA	X							X				X													
BASAL-CELL CARCINOMA																									
SMALL INTESTINE	+	-	+	+	+	+	-	+	A	A	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+
PAPILLARY ADENOMA			X																						
LARGE INTESTINE	+	-	-	+	+	+	-	+	A	A	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	-	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	A	A	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	+	-	+	A	A	+	+	+	+	-	-	+	+	-	-	-	-	-	-	+
ADRENAL	+	+	+	+	+	+	+	+	A	A	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+
THYROID	+	+	+	+	-	+	+	+	A	A	+	-	-	+	+	+	+	-	+	+	-	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	+	+	+	-	-	-	+	-	A	A	+	-	-	-	-	-	+	-	-	-	-	+	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	-	+	+	+	+	+	+	+	A	A	-	+	+	+	-	+	-	+	-	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	-	A	A	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																			X						
FIBROUS HISTIOCYTOMA, MALIGNANT																									
MALIGNANT LYMPHOMA, NOS								X																	

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	091	090	094	104	046	067	104	044	041	041	055	044	041	011	043	033	034	075	031	062	078	068	079	077	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	N		44M
FIBROMA	X																									1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	-	+	+	A	+		41
HEPATOCELLULAR CARCINOMA, METASTA	X																									2
ALVEOLAR/BRONCHIOLAR ADENOMA											X								X							4
ALVEOLAR/BRONCHIOLAR CARCINOMA													X													1
TRACHEA	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		41
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	-		40
SPLEEN	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	-		38
HEMANGIOMA																						X				2
LYMPH NODES	+	+	+	-	-	+	A	+	+	+	+	+	+	+	+	+	A	A	+	-	-	-	A	-		30
THYMUS	-	-	-	-	-	+	A	-	-	-	-	-	-	-	-	-	A	A	-	-	-	-	A	-		1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		43
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		43
LIVER	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		44
HEPATOCELLULAR ADENOMA									X											X						4
HEPATOCELLULAR CARCINOMA	X			X	X	X		X			X	X		X	X	X			X					X		26
HEMANGIOMA									X													X				3
HEMANGIOSARCOMA										X																1
BILE DUCT	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		44
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	N	N	A	+	N	+	+	N	+	+	N	N	A	A	N	+	N	+	N	A	N	44M
PANCREAS	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	-		38
ESOPHAGUS	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+		39
STOMACH	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	A	A	-	+	+	-	A	-		37
SQUAMOUS CELL PAPILLOMA		X																								3
BASAL-CELL CARCINOMA																										1
SMALL INTESTINE	+	-	+	-	+	-	A	+	+	+	+	-	+	+	-	+	A	A	-	+	-	-	+	A	-	30
PAPILLARY ADENOMA																										1
LARGE INTESTINE	+	-	+	-	-	-	A	+	+	+	+	+	+	+	-	+	A	A	-	-	-	-	A	-		27
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	-		40
URINARY BLADDER	+	+	+	-	+	+	A	-	+	+	+	+	+	+	-	+	A	A	+	+	+	+	A	-		38
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	-	+	-	A	+	+	+	+	-	-	-	+	+	A	A	-	-	+	+	A	-		25
ADRENAL	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	-		40
THYROID	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	A	A	+	+	-	+	+	A	+	37
FOLLICULAR-CELL ADENOMA			X																							1
PARATHYROID	+	-	-	-	-	+	A	+	+	-	-	-	+	-	-	-	A	A	-	-	-	-	+	A	-	14
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	N	N	N	N	A	N	N	N	N	N	N	N	N	N	A	A	N	N	N	N	N	A	N	44M
TESTIS	+	+	+	-	+	+	A	-	+	+	-	+	+	+	+	+	A	A	+	+	+	+	+	A	-	35
PROSTATE	-	+	+	-	+	+	A	-	+	+	+	+	+	+	-	+	A	A	-	+	-	+	-	A	-	32
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	A	A	N	N	N	N	N	A	N	44M
SARCOMA, NOS																						X				2
FIBROUS HISTIOCYTOMA, MALIGNANT			X																							1
MALIGNANT LYMPHOMA, NOS																										1

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	040	040	038	027	040	041	040	040	039	035	041	037	039	039	040	039	041	039	041	041	041	041	041	035	027
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
TRACHEA	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	A
SPLEEN	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
LYMPH NODES	+	-	+	A	+	-	-	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	A	A
THYMUS	-	+	-	A	-	-	-	-	-	-	+	A	-	-	-	-	+	-	-	+	-	+	-	A	A
CIRCULATORY SYSTEM																									
HEART	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	A	+	-	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	A
LIVER	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
HEPATOCELLULAR ADENOMA																X		X		X			X		
HEPATOCELLULAR CARCINOMA										X				X	X		X								
BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
GALLBLADDER & COMMON BILE DUCT	+	+	+	A	+	+	+	+	+	N	+	A	N	+	N	+	+	+	+	+	+	+	N	A	A
PANCREAS	+	+	+	A	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
ESOPHAGUS	+	+	-	A	+	+	-	-	-	+	+	A	+	+	+	-	+	+	+	+	+	+	+	A	A
STOMACH	+	+	-	A	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
SMALL INTESTINE	+	+	-	A	+	+	+	+	-	+	+	A	+	+	+	-	-	+	+	+	+	+	+	A	A
LARGE INTESTINE	+	+	-	A	+	+	+	+	-	-	+	A	-	+	+	-	+	+	+	+	+	+	+	A	A
URINARY SYSTEM																									
KIDNEY	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
URINARY BLADDER	+	-	+	A	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	A	A
ENDOCRINE SYSTEM																									
PITUITARY	-	+	-	A	-	+	+	+	+	-	+	A	-	+	-	+	+	+	+	+	+	-	-	A	A
ADENOMA, NOS																									
ADRENAL	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
THYROID	+	+	+	A	+	+	+	+	+	+	+	A	-	-	+	+	+	-	+	+	+	+	+	A	A
PARATHYROID	-	-	-	A	-	+	-	+	-	+	+	A	-	-	-	-	+	-	-	+	-	-	-	A	A
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	A	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	A	A
TESTIS	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A
PROSTATE	+	-	-	A	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	-	+	+	+	A	A

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	039	040	040	040	040	039	039	039	041	039	018	039	040	040	041	040	027	029	039	039	039	028	040	040	040	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	A	+	+	+	44
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	44
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	A	-	-	+	42
LYMPH NODES	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	A	-	+	+	37
THYMUS	-	-	-	-	-	-	+	-	+	-	-	-	+	-	-	-	-	-	-	-	+	A	-	-	-	9
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	41
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
HEPATOCELLULAR ADENOMA										X				X			X									7
HEPATOCELLULAR CARCINOMA								X															X	X		7
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	N	N	N	+	+	N	A	N	+	+	45M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	43
ESOPHAGUS	+	-	+	+	+	-	+	+	+	+	-	+	-	+	+	+	-	-	+	+	+	A	-	+	+	33
STOMACH	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	40
SMALL INTESTINE	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	-	+	+	37
LARGE INTESTINE	-	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	A	-	+	+	35
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
URINARY BLADDER	-	+	+	+	-	+	+	+	+	+	+	-	+	-	+	+	-	+	+	+	+	A	+	+	+	37
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	A	+	-	+	34
ADENOMA, NOS																	X									1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
THYROID	-	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	A	-	+	+	36
PARATHYROID	-	-	-	-	-	+	-	-	-	+	-	+	-	-	+	-	-	-	-	-	+	A	-	+	+	13
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	45M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	45
PROSTATE	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	38

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	100	104	104	106	101	098	099	106	104	104	104	104	101	089	104	104	104	104	104	104	104	104	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, METASTATIC																		X							
ALVEOLAR/BRONCHIOLAR ADENOMA																X			X						
ALVEOLAR/BRONCHIOLAR CARCINOMA																							X		
OSTEOSARCOMA, METASTATIC														X											
TRACHEA	+	-	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	-	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
MALIGNANT LYMPHOMA, NOS																									
LYMPH NODES	+	+	+	-	+	+	+	+	+	-	+	+	A	-	+	-	+	+	+	+	+	+	+	+	-
THYMUS	-	-	-	-	+	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	-	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																	X								
HEPATOCELLULAR CARCINOMA																		X							
LIPOMA				X																					
HEMANGIOSARCOMA										X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	N	+	+	N	+	N	A	+	+	+	+	+	+	+	+	N	+	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	-	+	+	+	+	-	+	+	A	+	+	+	+	-	+	+	-	+	+	+	+
STOMACH	-	+	+	+	-	+	+	+	+	-	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	-	+	+	+	-	+	+	+	-	-	+	-	A	-	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
LARGE INTESTINE	-	+	+	+	-	+	+	+	+	-	+	-	A	-	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA																									
URINARY SYSTEM																									
KIDNEY	+	-	+	+	+	+	+	+	+	-	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	+	+	+	+	+	+	-	+	-	+	-	A	-	-	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	-	+	+	+	+	+	-	+	+	A	+	-	+	+	-	+	+	-	-	+	-	-
ADENOMA, NOS												X											X		
ADRENAL	+	+	+	+	-	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA				X																			X		
PARATHYROID	-	+	-	-	-	-	-	-	-	-	-	-	A	+	-	-	-	-	-	-	-	-	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	N	+	+	+	N	+	N	+	N	A	N	N	N	+	+	+	N	+	N	+	N	N
UTERUS	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	-	+	+	+	+	+	-	+	-	+
OVARY	+	+	+	+	+	+	+	+	+	-	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+
CYSTADENOMA, NOS																	X								
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA																									
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA														X											
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS	X				X		X																		
SITE UNKNOWN													A												
CARCINOMA,NOS																		X							

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	07 6	07 7	07 8	07 9	08 0	08 1	08 2	08 3	08 4	08 5	08 6	08 7	08 8	08 9	09 0	09 1	09 2	09 3	09 4	09 5	09 6	09 7	09 8	09 9	10 0	TOTAL
WEEKS ON STUDY	08 9	10 4	04 4	04 4	04 4	04 4	04 4	04 4	04 4	04 4	09 3	04 4	04 4	04 4	06 5	07 6	04 4	04 4	04 4	04 4	09 4	04 4	04 4	04 4	08 5	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
CARCINOMA, NOS, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR ADENOMA													X													3
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
OSTEOSARCOMA, METASTATIC																										1
TRACHEA	A	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	A	-	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
SPLEEN	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
HEMANGIOSARCOMA																X										1
MALIGNANT LYMPHOMA, NOS				X																						1
LYMPH NODES	A	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	-	+	+	39
THYMUS	A	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	+	-	-	-	-	-	-	2
CIRCULATORY SYSTEM																										
HEART	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
DIGESTIVE SYSTEM																										
SALIVARY GLAND	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	-	+	+	+	-		43
LIVER	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	X	+	+	+	+	+	+	46
HEPATOCELLULAR ADENOMA																										2
HEPATOCELLULAR CARCINOMA																										1
LIPOMA																										1
HEMANGIOSARCOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	+	+	+	N	+	A	+	+	+	N	N	+	+	+	+	+	+	N	N	N	48*
PANCREAS	A	+	+	+	+	+	+	+	+	+	A	+	-	-	+	+	+	+	+	+	+	+	+	+	+	43
ESOPHAGUS	A	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	-	+	+	-	41
STOMACH	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	42
SMALL INTESTINE	A	+	+	+	+	+	+	+	+	+	A	+	+	+	-	-	+	+	+	+	+	+	+	+	+	39
MALIGNANT LYMPHOMA, NOS														X												1
LARGE INTESTINE	A	+	+	+	-	+	+	+	+	+	A	+	+	+	-	-	+	-	+	+	+	+	+	+	+	38
LEIOMYOMA																				X						1
URINARY SYSTEM																										
KIDNEY	A	+	+	+	+	+	+	+	+	-	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	42
URINARY BLADDER	A	+	+	+	+	+	+	+	+	+	A	+	+	+	-	-	+	+	+	+	+	+	+	+	+	39
ENDOCRINE SYSTEM																										
PITUITARY	A	+	+	+	+	+	+	-	-	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	35
ADENOMA, NOS				X			X																X			5
ADRENAL	A	+	+	+	+	-	+	+	+	+	A	+	-	+	+	+	-	+	+	+	+	+	+	+	+	41
THYROID	A	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA																										2
PARATHYROID	A	-	+	-	-	-	+	+	+	+	A	+	-	-	+	-	-	+	-	-	+	-	-	-	-	11
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	+	N	N	+	A	N	N	+	N	+	+	N	+	+	N	+	+	+	+	48*
UTERUS	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
OVARY	A	+	-	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	-	-	+	41
CYSTADENOMA, NOS																										1
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
PAPILLARY ADENOMA																X										1
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
OSTEOSARCOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
MALIGNANT LYMPHOMA, NOS													X					X			X				X	7
SITE UNKNOWN											A															
CARCINOMA,NOS																										1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	089	053	068	102	099	102	092	104	097	104	101	082	054	102	067	076	077	079	104	062	096	060	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
TRACHEA	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	-	+	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
SPLEEN	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	-	-	+	+	+	-	+
LYMPH NODES	+	+	-	+	-	-	+	-	-	+	-	+	-	+	A	+	A	A	-	-	+	-	+	-	-
THYMUS	-	-	-	+	-	-	-	-	-	-	-	-	-	-	A	-	A	A	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	+	+	+	+	-	+	+	+	+	+	+	-	+	A	+	A	A	+	+	+	+	+	-	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
HEPATOCELLULAR ADENOMA					X							X	X						X			X			X
HEPATOCELLULAR CARCINOMA		X	X	X		X		X	X	X	X									X	X		X		
LIPOMA																			X						
HEMANGIOMA							X																		
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
GALLBLADDER & COMMON BILE DUCT	+	N	N	+	N	N	+	N	+	+	N	+	+	N	A	+	A	A	N	+	+	N	+	N	N
PANCREAS	+	+	+	+	+	-	+	+	+	+	-	+	+	+	A	-	A	A	+	-	+	+	+	-	+
ESOPHAGUS	+	+	+	+	+	-	+	+	+	-	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
STOMACH	-	+	+	-	-	-	+	+	+	+	-	+	+	-	A	-	A	A	+	-	+	-	+	-	+
SQUAMOUS CELL PAPILLOMA																							X		
SMALL INTESTINE	+	+	+	-	-	-	+	+	+	-	-	+	+	-	A	-	A	A	+	-	+	-	+	-	+
LARGE INTESTINE	+	-	+	-	-	-	+	+	+	+	-	+	-	-	A	-	A	A	-	-	+	-	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
URINARY BLADDER	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	-	A	A	-	-	+	-	+	-	+
ENDOCRINE SYSTEM																									
PITUITARY	-	-	+	+	+	-	+	+	+	+	-	+	+	+	A	-	A	A	+	+	+	+	+	-	-
ADENOMA, NOS																					X				
ADRENAL	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	-	+
CORTICAL CARCINOMA																							X		
PHEOCHROMOCYTOMA																							X		
THYROID	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	-	+	-	+
FOLLICULAR-CELL ADENOMA											X														
PARATHYROID	+	+	+	+	-	-	+	-	+	-	-	+	-	A	+	A	A	-	-	-	-	+	-	+	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	+	N	N	+	N	+	N	+	A	N	A	A	N	N	+	N	N	N	N
UTERUS	-	+	+	+	+	-	+	+	+	-	+	+	+	A	+	A	A	-	-	+	+	+	-	-	
OVARY	+	-	+	+	+	-	+	-	+	+	+	+	+	+	A	+	A	A	+	-	+	+	+	-	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	A	A	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																X									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	087	073	082	103	056	072	104	071	058	675	095	084	102	077	064	095	062	097	080	084	104	104	090	101	102	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	A	+	+	+	-	+	+	+	A	A	+	+	+		+	+	+	+	+	+	+	A	41
HEPATOCELLULAR CARCINOMA, METASTA																X										1
TRACHEA	+	+	+	A	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	-	+	A	39
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	A	+	+	+	-	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A	40
SPLEEN	+	+	+	A	+	-	+	-	+	+	+	A	A	+	+	-	+	+	-	+	+	+	+	+	A	35
LYMPH NODES	+	+	+	A	-	-	+	-	+	+	-	A	A	-	-	+	-	-	-	+	+	-	+	-	A	20
THYMUS	-	-	-	A	-	-	-	-	-	-	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	1
CIRCULATORY SYSTEM																										
HEART	+	+	+	A	+	+	+	-	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A	41
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	A	+	+	-	+	+	-	+	A	A	+	+	+	+	-	+	+	+	+	+	+	A	36
LIVER	+	+	+	A	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A	42
HEPATOCELLULAR ADENOMA					X		X																			8
HEPATOCELLULAR CARCINOMA	X	X	X			X		X			X	X			X	X	X	X	X	X	X	X	X		X		28
LIPOMA																										1
HEMANGIOMA																										1
HEMANGIOSARCOMA														X												1
BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A	42
GALLBLADDER & COMMON BILE DUCT	N	+	+	A	N	N	+	+	+	N	N	A	A	+	N	N	+	N	N	+	+	+	+	+	A	43*
PANCREAS	+	+	+	A	+	-	+	-	+	+	+	A	A	+	+	-	+	+	-	-	+	+	+	+	A	33
ESOPHAGUS	+	+	+	A	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A	40
STOMACH	+	+	-	A	-	-	+	-	+	+	-	A	A	-	-	-	+	+	-	-	+	+	+	+	A	23
SQUAMOUS CELL PAPILLOMA																										1
SMALL INTESTINE	+	+	-	A	-	-	+	-	+	+	-	A	A	-	-	-	-	+	-	-	+	+	-	+	A	21
LARGE INTESTINE	+	+	-	A	-	-	+	-	+	+	-	A	A	-	+	+	-	+	-	-	+	+	-	+	A	21
URINARY SYSTEM																										
KIDNEY	+	+	+	A	+	+	+	-	+	+	+	A	A	+	+	+	+	+	-	+	+	+	+	+	A	39
URINARY BLADDER	+	+	+	A	+	-	+	-	-	+	+	A	A	+	+	+	-	+	-	+	+	+	+	+	A	32
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	A	-	+	+	-	+	-	+	A	A	-	+	-	+	+	+	+	-	-	+	+	A	29
ADENOMA, NOS							X																	X		3
ADRENAL	+	+	+	A	+	+	+	-	+	+	+	A	A	+	+	+	+	+	-	+	+	+	+	+	A	39
CORTICAL CARCINOMA																										1
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	A	-	+	+	+	+	+	+	A	A	+	+	+	-	+	+	+	+	+	+	+	A	38
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	+	+	A	-	-	-	+	-	-	+	A	A	+	-	-	-	-	+	+	-	-	+	+	A	21
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	A	+	N	N	N	+	N	N	A	A	N	N	N	N	N	N	N	+	+	N	N	A	43*
UTERUS	+	+	+	A	+	+	+	-	+	-	+	A	A	+	+	+	-	+	-	+	+	+	+	-	A	31
OVARY	+	+	+	A	+	-	+	-	+	+	+	A	A	+	+	+	+	+	-	+	+	+	+	-	A	34
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	A	N	N	N	N	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	A	43*
MALIGNANT LYMPHOMA, NOS	X																									2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF PENTACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	050	060	054	071	059	050	071	071	074	074	074	054	049	042	073	074	060	074	049	074	060	067	060	067	060
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	-
ALVEOLAR/BRONCHIOLAR ADENOMA										X															
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	-	+	+	A	+	+	+	+	+	A	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	A	+	+	+	+
LYMPH NODES	+	-	+	+	-	+	-	+	+	-	+	+	+	-	A	-	+	+	-	+	-	A	+	+	+
THYMUS	-	-	-	-	+	-	-	-	-	-	-	-	-	-	A	+	-	-	-	+	-	A	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	-	+	+	A	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+
HEPATOCELLULAR ADENOMA	X			X		X	X	X	X				X				X				X			X	
HEPATOCELLULAR CARCINOMA		X														X		X		X			X		X
MALIGNANT LYMPHOMA, NOS																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	+	N	+	N	N	+	N	+	+	N	N	+	A	N	+	+	N	+	N	A	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	A	+	+	+
ESOPHAGUS	+	+	-	+	+	+	-	+	+	+	+	-	+	+	A	+	+	-	+	+	+	A	+	+	+
STOMACH	+	-	-	+	-	+	+	-	+	+	+	-	+	-	A	+	+	-	-	+	-	A	-	-	-
PAPILLOMA, NOS						X																			
SQUAMOUS CELL PAPILLOMA																									
SMALL INTESTINE	-	-	-	-	-	+	-	-	+	+	+	-	+	-	A	+	+	+	-	+	-	A	-	-	-
LARGE INTESTINE	-	-	-	+	-	-	+	-	+	-	+	-	+	-	A	-	+	+	-	+	-	A	-	-	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	-	+	+
MALIGNANT LYMPHOMA, NOS																									
URINARY BLADDER	-	-	+	+	+	+	+	+	+	+	-	+	+	+	A	-	+	+	-	+	+	A	-	-	+
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	-	-	+	+	+	+	+	+	+	-	+	A	+	+	+	-	+	+	A	-	+	+
ADENOMA, NOS									X																
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+
THYROID	+	+	-	+	+	+	+	+	+	+	-	-	+	-	A	+	+	+	-	+	+	A	+	+	+
PARATHYROID	+	-	-	-	-	+	+	-	-	+	-	-	+	-	A	+	+	-	-	+	-	A	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	+	+	N	N	+	N	+	N	N	A	+	N	+	N	+	+	A	N	+	N
UTERUS	+	+	+	-	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	A	+	+	+
OVARY	+	+	-	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	A	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	A	N	N	N
MALIGNANT LYMPHOMA, NOS										X															

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	0076	0077	0078	0079	0080	0081	0082	0083	0084	0085	0086	0087	0088	0089	0090	0091	0092	0093	0094	0095	0096	0097	0098	0099	0100	TOTAL
WEEKS ON STUDY	049	071	040	071	074	071	040	038	060	057	054	054	050	054	054	074	049	074	074	062	074	060	060	067	074	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	-	+	+	A	+	+	+	+	+	+	+	+	+	-	-	A	+	41
ALVEOLAR/BRONCHIOLAR ADENOMA																			X						X	3
TRACHEA	+	-	-	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	-	+	+	+	-	A	+	39
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	-	+	+	+	+	+	A	+	+	-	A	+	+	+	+	+	+	+	+	-	+	-	A	+	40
SPLEEN	+	+	+	+	+	+	+	A	-	+	-	A	+	+	+	+	+	+	+	+	+	+	-	A	+	41
LYMPH NODES	+	-	+	+	+	-	-	A	+	-	-	A	-	+	+	-	-	+	+	-	+	-	-	A	+	26
THYMUS	-	-	-	-	-	-	-	A	-	-	-	A	-	-	-	-	-	-	-	+	-	-	-	A	+	5
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	A	-	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	+	43
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	-	-	A	+	41
LIVER	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	45
HEPATOCELLULAR ADENOMA			X	X			X			X								X			X				X	19
HEPATOCELLULAR CARCINOMA		X			X				X								X		X	X		X	X			13
MALIGNANT LYMPHOMA, NOS																										1
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	45
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	N	N	N	A	N	N	N	A	+	N	N	+	N	+	N	N	+	+	N	A	N	45*
PANCREAS	+	+	+	+	+	+	+	A	-	+	-	A	+	+	+	+	+	+	+	+	+	+	-	A	+	41
ESOPHAGUS	+	-	-	+	+	-	-	A	+	-	+	A	+	+	+	+	+	+	+	+	+	+	-	A	+	35
STOMACH	+	+	-	+	+	-	+	A	-	-	-	A	+	+	-	+	+	+	+	+	+	+	-	A	+	26
PAPILLOMA, NOS																										1
SQUAMOUS CELL PAPILLOMA																						X				1
SMALL INTESTINE	-	+	-	+	+	+	+	A	-	-	-	A	+	-	-	+	-	+	+	+	+	+	-	A	+	22
LARGE INTESTINE	-	+	-	+	+	+	+	A	-	-	-	A	+	-	-	+	-	+	+	+	+	+	-	A	+	21
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	+	43
MALIGNANT LYMPHOMA, NOS																									X	1
URINARY BLADDER	+	-	+	+	+	+	+	A	+	+	-	A	+	+	+	+	-	+	+	+	+	+	-	A	-	33
ENDOCRINE SYSTEM																										
PITUITARY	-	-	+	+	+	+	+	A	+	+	-	A	-	+	+	+	+	+	-	+	+	+	-	A	-	32
ADENOMA, NOS																										1
ADRENAL	+	-	+	+	+	-	-	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	+	41
THYROID	+	-	-	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	A	+	37
PARATHYROID	-	-	-	+	+	-	+	A	-	-	-	A	+	-	+	+	-	-	-	+	-	-	-	A	+	18
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	N	N	A	N	N	N	A	+	N	N	+	N	+	N	N	+	N	N	A	+	45*
UTERUS	+	-	+	+	+	+	+	A	+	+	-	A	+	+	+	+	+	-	+	+	+	+	-	A	+	39
OVARY	+	-	+	+	+	+	+	A	+	+	-	A	+	+	+	+	+	-	+	+	+	+	-	A	+	39
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	A	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	A	N	45*
MALIGNANT LYMPHOMA, NOS																										1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(50)
*ABSCESS, NOS			1 (2%)
HYPERPLASIA, PSEUDOEPITHELIOMATO			2 (4%)
*SUBCUT TISSUE	(50)	(49)	(50)
CHOLESTEROL DEPOSIT		1 (2%)	
RESPIRATORY SYSTEM			
#TRACHEAL GLAND	(50)	(47)	(49)
DILATATION, NOS	2 (4%)	1 (2%)	2 (4%)
#LUNG	(50)	(49)	(50)
EMPHYSEMA, ALVEOLAR	3 (6%)	1 (2%)	4 (8%)
CONGESTION, NOS	1 (2%)		1 (2%)
EDEMA, INTERSTITIAL		1 (2%)	
HEMORRHAGE	1 (2%)	2 (4%)	1 (2%)
INFLAMMATION, INTERSTITIAL	5 (10%)	10 (20%)	15 (30%)
PNEUMONIA, LIPID	1 (2%)		
ABSCESS, NOS	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	27 (54%)	31 (63%)	19 (38%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
INFLAMMATION PROLIFERATIVE	1 (2%)	2 (4%)	
#LUNG/ALVEOLI	(50)	(49)	(50)
EDEMA, NOS		1 (2%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(47)	(49)
HYPOPLASIA, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, DIFFUSE	1 (2%)		
HYPERPLASIA, HEMATOPOIETIC	2 (4%)		
#SPLEEN	(50)	(48)	(50)
FIBROSIS, FOCAL			1 (2%)
HYPERPLASIA, LYMPHOID	3 (6%)		1 (2%)
HEMATOPOIESIS		1 (2%)	2 (4%)
#SPLENIC CAPSULE	(50)	(48)	(50)
HEMORRHAGIC CYST	1 (2%)		
HYPERPLASIA, NOS			2 (4%)
#SPLENIC RED PULP	(50)	(48)	(50)
CONGESTION, NOS			2 (4%)
#LYMPH NODE	(46)	(40)	(46)
INFLAMMATION, ACUTE DIFFUSE		1 (3%)	
HYPERPLASIA, LYMPHOID		2 (5%)	
#MANDIBULAR L. NODE	(46)	(40)	(46)
INFLAMMATION, SEROUS			1 (2%)
INFLAMMATION, ACUTE SEROUS	1 (2%)		
#SACRAL LYMPH NODE	(46)	(40)	(46)
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(2)	(5)	(6)
HYPERPLASIA, LYMPHOID	1 (50%)		
CIRCULATORY SYSTEM			
#HEART	(50)	(49)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC FOCAL	5 (10%)	2 (4%)	2 (4%)
#LEFT AURICULAR APPEN	(50)	(49)	(50)
MINERALIZATION			1 (2%)
THROMBUS, MURAL			2 (4%)
#MYOCARDIUM	(50)	(49)	(50)
MINERALIZATION			1 (2%)
*AORTA	(50)	(49)	(50)
MINERALIZATION			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*PULMONARY ARTERY	(50)	(49)	(50)
MINERALIZATION		1 (2%)	1 (2%)
#PANCREAS	(48)	(48)	(50)
PERIARTERITIS	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
*INTESTINAL TRACT	(50)	(49)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
#SALIVARY GLAND	(49)	(47)	(49)
DILATATION/DUCTS	1 (2%)		1 (2%)
#LIVER	(50)	(48)	(50)
CYST, NOS	1 (2%)		
HEMORRHAGE	1 (2%)	1 (2%)	
INFLAMMATION, NECROTIZING	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	2 (4%)	1 (2%)	2 (4%)
NODULE			1 (2%)
CHOLANGIOFIBROSIS	3 (6%)		
DEGENERATION, GRANULAR		1 (2%)	
NECROSIS, FOCAL			2 (4%)
NECROSIS, LIQUEFACTIVE		1 (2%)	
METAMORPHOSIS FATTY	26 (52%)	29 (60%)	20 (40%)
#LIVER/CENTRILOBULAR	(50)	(48)	(50)
HEPATOCYTOMEGALY		1 (2%)	
#BILE DUCT	(50)	(48)	(50)
DILATATION, NOS	1 (2%)		
CYST, NOS	1 (2%)		
FIBROSIS, FOCAL		1 (2%)	
HYPERTROPHY, FOCAL	1 (2%)		
HYPERPLASIA, NOS	1 (2%)	2 (4%)	1 (2%)
HYPERPLASIA, FOCAL	18 (36%)	8 (17%)	8 (16%)
#PANCREAS	(48)	(48)	(50)
DILATATION/DUCTS		1 (2%)	
HYPERPLASIA, NODULAR	9 (19%)	4 (8%)	3 (6%)
#PANCREATIC ACINUS	(48)	(48)	(50)
NECROSIS, FOCAL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, FOCAL	10 (21%)	3 (6%)	3 (6%)
HYPERPLASIA, NODULAR	2 (4%)	6 (13%)	4 (8%)
#STOMACH	(46)	(43)	(42)
ULCER, ACUTE			1 (2%)
PARASITISM	1 (2%)		
#GASTRIC MUCOSA	(46)	(43)	(42)
MINERALIZATION			1 (2%)
DILATATION, NOS	1 (2%)		1 (2%)
#FORESTOMACH	(46)	(43)	(42)
INFLAMMATION, CHRONIC DIFFUSE			1 (2%)
HYPERPLASIA, PSEUDOEPITHELIOMATO			1 (2%)
#DUODENUM	(46)	(40)	(39)
INFLAMMATION, ACUTE/CHRONIC	3 (7%)	2 (5%)	1 (3%)
#COLON	(46)	(38)	(38)
NEMATODIASIS			1 (3%)
PARASITISM	1 (2%)	3 (8%)	
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(50)
CAST, NOS			1 (2%)
INFLAMMATION, DIFFUSE			2 (4%)
INFLAMMATION, INTERSTITIAL	3 (6%)	12 (24%)	2 (4%)
INFLAMMATION, CHRONIC	3 (6%)	8 (16%)	3 (6%)
INFLAMMATION, CHRONIC DIFFUSE	4 (8%)	14 (29%)	33 (66%)
HYPERPLASIA, TUBULAR CELL			1 (2%)
#RENAL PAPILLA	(50)	(49)	(50)
MINERALIZATION	4 (8%)	29 (59%)	29 (58%)
#KIDNEY/TUBULE	(50)	(49)	(50)
DILATATION, NOS	2 (4%)	12 (24%)	2 (4%)
CAST, NOS	12 (24%)	18 (37%)	1 (2%)
PIGMENTATION, NOS		2 (4%)	
REGENERATION, NOS	1 (2%)		
#KIDNEY/PELVIS	(50)	(49)	(50)
MINERALIZATION	1 (2%)	1 (2%)	
HYPERPLASIA, EPITHELIAL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#URINARY BLADDER	(47)	(44)	(48)
HEMORRHAGE			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(46)	(46)
CYST, NOS	1 (2%)	1 (2%)	
MULTIPLE CYSTS	1 (2%)		1 (2%)
CONGESTION, NOS	1 (2%)		
HEMORRHAGE			1 (2%)
HEMORRHAGIC CYST	1 (2%)		1 (2%)
HEMOSIDEROSIS	1 (2%)		1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL	2 (4%)		
ANGIECTASIS	1 (2%)	1 (2%)	
#ADRENAL	(49)	(48)	(50)
HEMORRHAGIC CYST			1 (2%)
NECROSIS, LIQUEFACTIVE		1 (2%)	
METAMORPHOSIS FATTY	3 (6%)	3 (6%)	3 (6%)
#ADRENAL CORTEX	(49)	(48)	(50)
HYPERPLASIA, NODULAR	1 (2%)		
#THYROID	(50)	(45)	(46)
ULTIMOBRANCHIAL CYST	2 (4%)		1 (2%)
MINERALIZATION			2 (4%)
GOITER, COLLOID STORAGE	1 (2%)		
HYPERPLASIA, FOCAL	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(50)
LACTATION		2 (4%)	1 (2%)
*PREPUTIAL GLAND	(50)	(49)	(50)
ULCER, ACUTE			1 (2%)
#PROSTATE	(47)	(43)	(47)
INFLAMMATION, FOCAL GRANULOMATOU			2 (4%)
#TESTIS	(49)	(47)	(49)
EDEMA, INTERSTITIAL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE	1 (2%)		
ABSCESS, NOS	1 (2%)		
FIBROSIS, DIFFUSE			1 (2%)
HEMOSIDEROSIS			1 (2%)
ATROPHY, NOS	6 (12%)	2 (4%)	2 (4%)
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	
#TESTIS/TUBULE	(49)	(47)	(49)
MINERALIZATION	3 (6%)	1 (2%)	1 (2%)
ATROPHY, FOCAL	8 (16%)	4 (9%)	2 (4%)
ATROPHY, DIFFUSE	13 (27%)	14 (30%)	13 (27%)
*VAS DEFERENS	(50)	(49)	(50)
SPERMATOCELE		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(47)	(49)
HYDROCEPHALUS, INTERNAL	1 (2%)		
SPONGIOSIS			1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
#CEREBELLAR WHITE MAT	(50)	(47)	(49)
EXTRACELLULAR VACUOLE ALTERATION	9 (18%)	3 (6%)	6 (12%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(49)	(50)
SYNECHIA, POSTERIOR	2 (4%)		
CATARACT	1 (2%)		
PHTHISIS BULBI	1 (2%)		
*EYE ANTERIOR CHAMBER	(50)	(49)	(50)
HEMORRHAGE		1 (2%)	
*SCLERA	(50)	(49)	(50)
MINERALIZATION	2 (4%)		
*EYE/CORNEA	(50)	(49)	(50)
VASCULARIZATION	2 (4%)		
*EYEBALL TUNICA VASCU	(50)	(49)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*EYE/CRYSTALLINE LENS	(50)	(49)	(50)
MINERALIZATION	6 (12%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
*ABDOMINAL MUSCLE	(50)	(49)	(50)
INFLAMMATION, CHRONIC NECROTIZIN	1 (2%)		
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(49)	(50)
NECROSIS, FAT			1 (2%)
*EPICARDIUM	(50)	(49)	(50)
INFLAMMATION, CHRONIC DIFFUSE	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		1	2
AUTOLYSIS/NO NECROPSY		1	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	49	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	48
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(49)	(48)
INFLAMMATION, GRANULOMATOUS			1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(44)	(46)	(46)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		1 (2%)
#TRACHEAL GLAND	(44)	(46)	(46)
DILATATION, NOS		1 (2%)	1 (2%)
#LUNG	(49)	(49)	(48)
EMPHYSEMA, ALVEOLAR	3 (6%)		4 (8%)
CONGESTION, NOS			1 (2%)
HEMORRHAGE			3 (6%)
INFLAMMATION, INTERSTITIAL	15 (31%)	7 (14%)	6 (13%)
PNEUMONIA, LIPID	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE FOCAL	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	26 (53%)	23 (47%)	18 (38%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC DIFFUSE	1 (2%)		
#LUNG/ALVEOLI	(49)	(49)	(48)
EDEMA, NOS			1 (2%)
HEMORRHAGE		1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(48)	(47)	(45)
CONGESTION, NOS		3 (6%)	
FIBROSIS, FOCAL		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMOSIDEROSIS	2 (4%)	3 (6%)	1 (2%)
HYPERPLASIA, RETICULUM CELL		2 (4%)	
HYPERPLASIA, LYMPHOID	1 (2%)		
HEMATOPOIESIS	2 (4%)		
#SPLENIC RED PULP	(48)	(47)	(45)
CONGESTION, NOS	2 (4%)	1 (2%)	1 (2%)
HEMOSIDEROSIS	1 (2%)	4 (9%)	1 (2%)
#LYMPH NODE	(42)	(41)	(41)
INFLAMMATION, ACUTE SEROUS	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)
CIRCULATORY SYSTEM			
#HEART	(49)	(49)	(48)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)	2 (4%)	
INFLAMMATION, CHRONIC FOCAL	2 (4%)	1 (2%)	
#PANCREAS	(49)	(47)	(46)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(48)	(45)
INFLAMMATION, NECROTIZING	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	3 (6%)	2 (4%)	
NODULE	1 (2%)	2 (4%)	2 (4%)
CHOLANGIOFIBROSIS	2 (4%)	2 (4%)	1 (2%)
METAMORPHOSIS FATTY	4 (8%)	5 (10%)	4 (9%)
ANGIECTASIS			1 (2%)
#BILE DUCT	(49)	(48)	(45)
HYPERPLASIA, NOS	1 (2%)	2 (4%)	
HYPERPLASIA, FOCAL	5 (10%)	3 (6%)	2 (4%)
HYPERPLASIA, DIFFUSE	1 (2%)		
#PANCREAS	(49)	(47)	(46)
DILATATION/DUCTS			1 (2%)
HYPERPLASIA, NODULAR		1 (2%)	
#PANCREATIC ACINUS	(49)	(47)	(46)
ATROPHY, FOCAL	3 (6%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NODULAR			1 (2%)
#STOMACH	(45)	(48)	(39)
ULCER, ACUTE		1 (2%)	
#GASTRIC MUCOSA	(45)	(48)	(39)
DILATATION, NOS		2 (4%)	2 (5%)
EXTRACELLULAR VACUOLE ALTERATION			2 (5%)
#DUODENUM	(45)	(44)	(38)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)		
INFLAMMATION, CHRONIC DIFFUSE		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(44)	(47)	(45)
CAST, NOS			1 (2%)
INFLAMMATION, INTERSTITIAL	2 (5%)	4 (9%)	2 (4%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
INFLAMMATION, CHRONIC DIFFUSE			4 (9%)
NEPHROSIS, NOS	1 (2%)		
#KIDNEY/CORTEX	(44)	(47)	(45)
CYST, NOS	1 (2%)		
#RENAL PAPILLA	(44)	(47)	(45)
MINERALIZATION		2 (4%)	1 (2%)
#KIDNEY/TUBULE	(44)	(47)	(45)
CAST, NOS		1 (2%)	3 (7%)
DEGENERATION, HYALINE		1 (2%)	
HEMOSIDEROSIS	1 (2%)	1 (2%)	2 (4%)
#KIDNEY/PELVIS	(44)	(47)	(45)
HYPERPLASIA, EPITHELIAL		1 (2%)	
#URINARY BLADDER	(45)	(41)	(37)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#U. BLADDER/MUCOSA	(45)	(41)	(37)
HYPERPLASIA, DIFFUSE	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(46)	(45)
CYST, NOS		2 (4%)	3 (7%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MULTIPLE CYSTS	1 (2%)	5 (11%)	5 (11%)
CONGESTION, NOS			1 (2%)
HEMORRHAGE	1 (2%)		
HEMORRHAGIC CYST	2 (4%)	2 (4%)	
INFLAMMATION, INTERSTITIAL		1 (2%)	
#PITUITARY/BASOPHIL	(49)	(46)	(45)
HYPERPLASIA, FOCAL	1 (2%)		
#ADRENAL	(48)	(49)	(46)
HEMORRHAGE		2 (4%)	
HEMORRHAGIC CYST	1 (2%)	1 (2%)	
NECROSIS, FOCAL			1 (2%)
METAMORPHOSIS FATTY	4 (8%)	4 (8%)	2 (4%)
#THYROID	(46)	(48)	(45)
GOITER NODULAR		1 (2%)	
HYPERPLASIA, FOCAL	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(49)	(48)
GALACTOCELE		1 (2%)	
LACTATION	20 (41%)	12 (24%)	12 (25%)
#UTERUS	(45)	(48)	(40)
DILATATION, NOS	1 (2%)		
HYDROMETRA			6 (15%)
HEMOSIDEROSIS	1 (2%)		
ADENOMYOSIS		1 (2%)	
#UTERUS/ENDOMETRIUM	(45)	(48)	(40)
CYST, NOS		1 (2%)	
HYPERPLASIA, CYSTIC	1 (2%)	1 (2%)	
#OVARY	(47)	(48)	(45)
CYST, NOS		2 (4%)	1 (2%)
MULTIPLE CYSTS		1 (2%)	
NERVOUS SYSTEM			
#CEREBRUM	(42)	(46)	(46)
HYDROCEPHALUS, INTERNAL			2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#BRAIN	(42)	(46)	(46)
COMPRESSION			1 (2%)
HYDROCEPHALUS, INTERNAL	1 (2%)	1 (2%)	
HEMORRHAGE	1 (2%)		
#CEREBELLAR WHITE MAT	(42)	(46)	(46)
EXTRACELLULAR VACUOLE ALTERATION	3 (7%)	3 (7%)	9 (20%)
#RAPHE MEDULLA OBLONG	(42)	(46)	(46)
EXTRACELLULAR VACUOLE ALTERATION		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(49)	(49)	(48)
INFLAMMATION, CHRONIC DIFFUSE	1 (2%)		
CATARACT	1 (2%)		
*EYE/CRYSTALLINE LENS	(49)	(49)	(48)
MINERALIZATION	5 (10%)	1 (2%)	
DEGENERATION, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PLEURA	(49)	(49)	(48)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(49)	(48)
CONGESTION, NOS			1 (2%)
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		1	2

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
AUTOLYSIS/NO NECROPSY	1	1	2

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	44	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	44	45
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS	(47)	(41)	(44)
INFLAMMATION, ACUTE			1 (2%)
#LUNG	(47)	(41)	(44)
INFLAMMATION, NOS	1 (2%)	2 (5%)	
INFLAMMATION, ACUTE	1 (2%)		
HEMATOPOIETIC SYSTEM			
#SPLEEN	(46)	(38)	(42)
HYPERPLASIA, LYMPHOID		1 (3%)	
#MANDIBULAR L. NODE	(38)	(30)	(37)
HYPERPLASIA, LYMPHOID		2 (7%)	
CIRCULATORY SYSTEM			
#HEART	(47)	(43)	(45)
PERIARTERITIS	1 (2%)		
ARTERIOSCLEROSIS, NOS	1 (2%)		
#MYOCARDIUM	(47)	(43)	(45)
INFLAMMATION, FOCAL		1 (2%)	
#LIVER	(48)	(44)	(45)
THROMBOSIS, NOS		2 (5%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#THYROID	(45)	(37)	(36)
ARTERIOSCLEROSIS, NOS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(48)	(44)	(45)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, FOCAL		3 (7%)	
INFLAMMATION, DIFFUSE		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		
NECROSIS, NOS		1 (2%)	1 (2%)
NECROSIS, FOCAL		4 (9%)	2 (4%)
NECROSIS, DIFFUSE		2 (5%)	
NECROSIS, HEMORRHAGIC			1 (2%)
METAMORPHOSIS FATTY	14 (29%)	9 (20%)	22 (49%)
CYTOPLASMIC VACUOLIZATION		1 (2%)	
BASOPHILIC CYTO CHANGE	1 (2%)		
CLEAR-CELL CHANGE	1 (2%)	1 (2%)	1 (2%)
CYTOLOGIC ALTERATION, NOS		1 (2%)	
HEPATOCYTOMEGALY		6 (14%)	
ANGIECTASIS		1 (2%)	
*GALLBLADDER	(48)	(44)	(45)
DILATATION, NOS		1 (2%)	
#STOMACH	(46)	(37)	(40)
ULCER, NOS		2 (5%)	
INFLAMMATION, FOCAL		1 (3%)	
#GASTRIC MUCOSA	(46)	(37)	(40)
HYPERPLASIA, FOCAL	1 (2%)	3 (8%)	
#FORESTOMACH	(46)	(37)	(40)
INFLAMMATION, CHRONIC FOCAL		1 (3%)	
HYPERPLASIA, EPITHELIAL		1 (3%)	
HYPERKERATOSIS		1 (3%)	
URINARY SYSTEM			
#KIDNEY	(47)	(40)	(45)
HYDRONEPHROSIS		1 (3%)	
INFLAMMATION, FOCAL		1 (3%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC		2 (5%)	
INFLAMMATION, CHRONIC DIFFUSE		1 (3%)	
METAMORPHOSIS FATTY	1 (2%)		
#URINARY BLADDER	(43)	(38)	(37)
INFLAMMATION, CHRONIC		1 (3%)	
ENDOCRINE SYSTEM			
#THYROID	(45)	(37)	(36)
HEMORRHAGE		1 (3%)	
#PANCREATIC ISLETS	(46)	(38)	(43)
HYPERPLASIA, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*SEMINAL VESICLE	(48)	(44)	(45)
DILATATION, NOS	1 (2%)		
#TESTIS	(46)	(35)	(45)
ATROPHY, NOS	1 (2%)		
ATROPHY, FOCAL	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(46)	(39)	(44)
HEMORRHAGE		1 (3%)	
INFLAMMATION, ACUTE		1 (3%)	
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(48)	(44)	(45)
EDEMA, NOS	1 (2%)		
FIBROSIS	1 (2%)		
DEGENERATION, CYSTIC	1 (2%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(48)	(44)	(45)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	13		14
AUTOLYSIS/NO NECROPSY	2	6	5

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	43	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	43	45
INTEGUMENTARY SYSTEM			
*SKIN	(48)	(43)	(45)
INFLAMMATION, FOCAL		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(46)	(41)	(41)
HEMORRHAGE		2 (5%)	
INFLAMMATION, NOS	1 (2%)		
INFLAMMATION, ACUTE			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(43)	(45)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
#SPLEEN	(45)	(35)	(41)
ABSCESS, NOS	1 (2%)		
HYPERPLASIA, LYMPHOID	5 (11%)	3 (9%)	2 (5%)
#LYMPH NODE	(39)	(20)	(26)
HYPERPLASIA, LYMPHOID	1 (3%)		
#MANDIBULAR L. NODE	(39)	(20)	(26)
HEMOSIDEROSIS		1 (5%)	
HYPERPLASIA, LYMPHOID		1 (5%)	
#PEYER'S PATCH	(39)	(21)	(22)
HYPERPLASIA, LYMPHOID	1 (3%)		
#KIDNEY	(42)	(39)	(43)
HYPERPLASIA, LYMPHOID	1 (2%)	1 (3%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#BRAIN	(43)	(39)	(44)
PERIVASCULITIS		1 (3%)	
#HEART	(46)	(41)	(43)
MINERALIZATION		2 (5%)	
THROMBOSIS, NOS		1 (2%)	
INFLAMMATION, ACUTE		1 (2%)	
*AORTA	(48)	(43)	(45)
MINERALIZATION		1 (2%)	
#UTERUS	(43)	(31)	(39)
THROMBOSIS, NOS		2 (6%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(43)	(36)	(41)
INFLAMMATION, CHRONIC			1 (2%)
#LIVER	(46)	(42)	(45)
HAMARTOMA	1 (2%)		
HEMORRHAGE		4 (10%)	
INFLAMMATION, NOS		2 (5%)	
INFLAMMATION, FOCAL	3 (7%)		
INFLAMMATION, DIFFUSE	1 (2%)		1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
NECROSIS, NOS		5 (12%)	
NECROSIS, FOCAL	1 (2%)	4 (10%)	4 (9%)
NECROSIS, DIFFUSE		2 (5%)	
METAMORPHOSIS FATTY		18 (43%)	28 (62%)
CYTOPLASMIC VACUOLIZATION	1 (2%)		
FOCAL CELLULAR CHANGE			1 (2%)
CLEAR-CELL CHANGE			4 (9%)
CYTOLOGIC ALTERATION, NOS	1 (2%)	1 (2%)	
HEPATOCYTOMEGALY		1 (2%)	2 (4%)
ANGIECTASIS			1 (2%)
#LIVER/HEPATOCYTES	(46)	(42)	(45)
MITOTIC ALTERATION	1 (2%)		
ATROPHY, FOCAL		1 (2%)	
#PANCREAS	(43)	(33)	(41)
DILATATION/DUCTS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC ACINUS	(43)	(33)	(41)
ATROPHY, NOS	1 (2%)		
#STOMACH	(42)	(23)	(26)
ULCER, NOS		2 (9%)	
INFLAMMATION, FOCAL		1 (4%)	
NECROSIS, FOCAL		1 (4%)	
HYPERPLASIA, EPITHELIAL			1 (4%)
#GASTRIC MUCOSA	(42)	(23)	(26)
HYPERPLASIA, FOCAL		3 (13%)	
#DUODENUM	(39)	(21)	(22)
ABSCESS, NOS		1 (5%)	
URINARY SYSTEM			
#KIDNEY	(42)	(39)	(43)
MINERALIZATION		1 (3%)	
HYDRONEPHROSIS		1 (3%)	
INFLAMMATION, CHRONIC		4 (10%)	
HEMOSIDEROSIS		1 (3%)	
#URINARY BLADDER	(39)	(32)	(33)
INFLAMMATION, NOS		1 (3%)	
INFLAMMATION, FOCAL		1 (3%)	
HYPERPLASIA, EPITHELIAL		1 (3%)	
ENDOCRINE SYSTEM			
#PITUITARY	(35)	(29)	(32)
NECROSIS, FOCAL		1 (3%)	
ANGIECTASIS	2 (6%)		
#ADRENAL	(41)	(39)	(41)
CYST, NOS	1 (2%)		
CONGESTION, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(48)	(43)	(45)
LACTATION	2 (4%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#UTERUS	(43)	(31)	(39)
HYDROMETRA			4 (10%)
CYST, NOS		1 (3%)	1 (3%)
INFLAMMATION, NOS	1 (2%)		
#UTERUS/ENDOMETRIUM	(43)	(31)	(39)
HYPERPLASIA, CYSTIC	31 (72%)	5 (16%)	6 (15%)
#OVARY	(41)	(34)	(39)
CYST, NOS	4 (10%)	5 (15%)	3 (8%)
INFLAMMATION, CHRONIC	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(43)	(39)	(44)
MALACIA		1 (3%)	
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(48)	(43)	(45)
ULCER, NOS		1 (2%)	
*EYE/LACRIMAL GLAND	(48)	(43)	(45)
DEGENERATION, CYSTIC	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(48)	(43)	(45)
STEATITIS	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	1	2

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
AUTO/NECROPSY/HISTO PERF	1		
AUTOLYSIS/NO NECROPSY	2	7	5

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

ANALYSIS OF PENTACHLOROETHANE
(LOT NO. CO41676)
MIDWEST RESEARCH INSTITUTE
(13-WEEK STUDY)

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	11.87	0.50	87.63
Determined	11.77	0.60	87.60
	11.97	0.64	87.78

B. WATER ANALYSIS

(Karl Fisher) 0.0099% ±0.0003 (δ)%

C. BOILING POINT

Determined

b.p.: 158°C at 742 mm (visual, microboiling point)

Literature Value

162.00°C
(Timmermans and Martin, 1926)

D. INDEX OF REFRACTION

Determined

n_D^{15}: 1.5043

Literature Value

1.50542
(Timmermans and Martin, 1926)

E. DENSITY

Determined

d_{23}^{27}: 1.6689

Literature Value

d^{30}: 1.6653
(Timmermans and Martin, 1926)

F. VAPOR-PHASE CHROMATOGRAPHY

Instrument: Tracor MT 220
Detection: Flame ionization
Inlet temperature: 200°C
Detector temperature: 270°C

(1) Detection of impurities

(a) System 1

Column: 10% Carbowax 20 M on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D., glass

Oven temperature program: 10 min. at 50°C, then 50 to 200°C at 10°C/min.

RESULTS: Major peak and six impurities (Table E1)

(b) System 2

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 3 m x 2 mm I.D., stainless steel

Oven temperature program: 10 min. at 50°C, then 50 to 200°C at 10°C/min.

RESULTS: Major peak and four impurities (Table E2)

TABLE E1. VAPOR-PHASE CHROMATOGRAPHY DATA: SYSTEM 1

Peak	Retention Time (min.)	Retention Time (Relative to Pentachloroethane)	Area (Percent of Pentachloroethane)
1	0.8	0.04	<0.05 (trace)
2	3.0	0.18	1.50 *(a)*
3	13.6	0.80	<0.05 (trace)
4	16.0	0.95	0.80 *(a)*
5	16.8	1.00	100
6	17.7	1.06	<0.05 (trace)
7	19.0	1.13	<0.05 (trace)

(a) Vapor-phase chromatography/mass spectrometry indicated that these peaks had mass fragmentation patterns identical to those in the literature for tetrachloroethylene. See Section F-2-C and F-2-D, Systems 3 and 4 for quantitation of Peak 2 and the explanation of Peak 4 (System 1).

TABLE E2. VAPOR-PHASE CHROMATOGRAPHY DATA: SYSTEM 2

Peak	Retention Time (min.)	Retention Time (Relative to Pentachloroethane)	Area (Percent of Pentachloroethane)
1	12.0	0.77	1.6 *(a)*
2	13.5	0.87	<0.005 (trace)
3	15.6	1.00	100
4	16.6	1.07	<0.005 (trace)
5	17.4	1.12	4.5

(a) Vapor-phase chromatography/mass spectrometry indicated that this peak had mass fragmentation patterns identical to those in the literature for tetrachloroethylene. See Section F-2-D for quantitation of Peak 1.

(2) Identification and quantitation of impurities

(a) System 1 (Trichloroethylene)

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 3 m x 2 mm I.D., stainless steel

Oven temperature program: 50°C, isothermal

A standard solution was injected containing 0.01% v/v trichloroethylene in o-dichlorobenzene. Trichloroethylene had a retention time of 10.8 minutes. The same amount of pentachloroethane was injected under the same conditions. A peak was observed at a retention time of 11.3 minutes, but its area was less than that of the trichloroethylene standard

CONCLUSION: Trichloroethylene *was not present* in the sample at concentrations >0.01%.

(b) System 2 (1,1,1,2- and 1,1,2,2-tetrachloroethane and hexachloroethane)

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 3 m x 2 mm I.D., stainless steel

Oven temperature program: 100°C, isothermal

Standard solutions were injected containing 0.01% v/v 1,1,1,2- and 1,1,2,2-tetrachloroethane in hexane and 50.1 mg/ml hexachloroethane in hexane. 1,1,1,2-Tetrachloroethane had a retention time of 6.0 minutes; 1,1,2,2-tetrachloroethane of 7.8 minutes; and hexachloroethane of 21.6 minutes. The same amount of pentachloroethane was injected under the same conditions. Peaks were observed at retention times of 6.1, 7.8, and 22.0 minutes. The peaks at 6.1 and 7.8 minutes were less intense than the tetrachloroethane standards. The peak at 22.0 minutes was enhanced by addition of known hexachloroethane and was therefore quantitated against the hexachloroethane standard.

CONCLUSION: 1,1,1,2-Tetrachloroethane was *not present* in the sample at concentrations >0.01%. 1,1,2,2-Tetrachloroethane was *not present* in the sample at concentrations >0.01%. Hexachloroethane was *present* in the sample at a concentration of 10.4% (w/v).

(c) System 3 (Identification of Peak 4, System 1)

Column: 10% Carbowax 20 M on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D., glass

Oven temperature program: 50°C, 5 min.; 50 to 150°C, 10°C/min.

On injection of varying volumes of pentachloroethane, all peaks except Peak 4 increased linearly with the volume injected. The area of Peak 4 increased to a constant area and remained unchanged with increased volume injections. The sample spiked with tetrachloroethylene showed an enhanced Peak 2 but no increase in the area of the fourth peak.

CONCLUSION: Peak 4, System 1, was due to column decomposition. Inlet decomposition was ruled out because spiked samples showed enhancement of Peak 2, not Peak 4. Detector decomposition was ruled out because both flame ionization detection and ion current detection showed the presence of Peak 4.

(d) System 4 (Tetrachloroethylene)

Inlet temperature: 75°C, 125°C, 200°C

Column and oven temperature program: Same as in System 3 above

The tetrachloroethylene—Peak 2, Section F-1-(a) Table E1 and Peak 1, Section F-1-(b)Table E2—in the pentachloroethane sample was quantitated against a standard at three inlet temperatures (75°C, 125°C, and 200°C). On plotting concentration versus inlet temperature, a straight line was obtained. The quantity of tetrachloroethylene was reported as that calculated for the inlet at 25°C.

CONCLUSION: The calculated concentration of tetrachloroethylene in the pentachloroethylene sample with the inlet at 25°C is 0.55%.

APPENDIX E

G. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

Instrument: Varian MAT CH4B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT 2000 MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.

(1) Detection of trichloroethylene, 1,1,1,2-tetrachloroethane, 1,1,2,2-tetrachloroethane and hexachloroethane

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 3 m x 2 mm I.D., stainless steel

Inlet temperature: 155°C

Oven temperature program: 16 min. at 80°C, then 80 to 110°C at 10°C/min.

A standard was injected containing (0.01% v/v) trichloroethylene, (0.01% v/v) 1,1,1,2-tetrachloroethane, (0.01% v/v) 1,1,2,2-tetrachloroethane, and (0.01% v/v) hexachloroethane in pentane. Strong ion current monitor peaks were observed for each standard. The pentachloroethane sample chromatogram indicated ion monitor peaks that corresponded to 1,1,2,2-tetrachloroethane (less intense than the standard) and hexachloroethane (more intense than the standard). A computer search was also made for two ions characteristic of the mass fragmentation pattern of each standard: 130, 132 for trichloroethylene; 131, 131 for 1,1,1,2-tetrachloroethane; 83, 85 for 1,1,2,2-tetrachloroethane; and 201, 203 for hexachloroethane.

CONCLUSION: Trichloroethylene was *not present* at concentrations $> 0.01\%$. 1,1,1,2-Tetrachloroethane was *not present* at concentrations $> 0.01\%$. 1,1,2,2-Tetrachloroethane was *present* but at a concentration $< 0.01\%$. Hexachloroethane was *present* at a concentration $> 0.01\%$.

(2) Identification of impurities

(a) System 1 (Same system as that employed in G-1)

The results are given in Table E3. Nine impurity peaks were detected. Three of these were large enough to give good mass fragmentation data.

(b) System 2

Column: 10% Carbowax 20 M on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D.

Inlet temperature: 155°C

Oven temperature program: 10 min. at 50°C, then 50 to 150°C at 10°C/min.

The results are given in Table E4. Eight impurities were detected on the ion current monitor, but only the two tetrachloroethylene peaks were large enough to give good mass fragmentation data.

TABLE E3. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY DATA: SP 2100/CARBOWAX COLUMN

Peak No.	Peak No. in Table E2	Retention Time (min.)	Mass	Percent of Base Peak	Normalized Percent of Base Peak	Assignment	Literature Mass	Spectrum Percent of Base Peak	Reference
1		1.8	Fragments				Fragments		
2		2.8							
3		3.1							
4		4.4							
5		6.0							
6	1	8.3	168	49	49	Tetrachloroethylene	168	48	(Eight peak index of mass spectra)
			166	100	100		166	100	
			164	79	79		164	78	
			133	25	25		133	20	
			131	71	71		131	62	
			129	84	84		129	64	
			96	17	17		96	14	
			94	25	25		94	21	
7		9.9							
8	2	13.2	168	19	19	1,1,2,2-	168	8	(Eight peak index of mass spectra)
			131	2	2	Tetrachloroethane	131	8	
			95	14	14		95	11	
			87	8	8		87	10	
			85	58	58		85	63	
			83	100	100		83	100	
			61	8	8		61	8	
			60	7	7		60	8	
9	3	19-22	169	18	45	Pentachloroethane	169	48	(Eight peak index of mass spectra)
			167	41	100		167	100	
			166	6	15		166	60	
			165	24	57		165	78	
			164	3	60		164	46	
			119	41	100		119	97	
			117	47	115		117	99	
			82	2	5		82	61	
10	5	26.3	203	49	82	Hexachloroethane	203	51	(Eight peak index of mass spectra)
			201	60	100		201	81	
			199	42	70		199	49	
			166	58	97		166	42	
			164	42	69		164	32	
			121	15	25		121	31	
			119	59	98		119	97	
			117	60	100		117	100	

TABLE E4. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY DATA: CARBOWAX 20 M COLUMN

Peak No.	Peak No. in Table E1	Retention Time (min.)	Mass	Percent of Base Peak	Normalized Percent of Base Peak	Assignment	Literature Mass	Spectrum Percent of Base Peak	Reference
1	1	1.2	Fragments				Fragments		
2		2.0							
3		2.7							
4	2	3.1	168	50	50	Tetrachloroethylene	168	48	(Eight peak index of mass spectra)
			166	100	100		166	100	
			164	60	60		164	78	
			133	15	15		133	20	
			131	58	58		131	65	
			129	60	60		129	64	
			96	14	14		96	20	
5		3.7							
6	4	16.4	168	50	50	Tetrachloroethylene	168	48	(Eight peak index of mass spectra)
			166	100	100		166	100	
			164	97	97		164	78	
			133	24	24		133	20	
			131	84	84		131	65	
			129	69	69		129	64	
			96	18	18		96	20	
			94	25	25				
7	5	17-19	169	18	49	Pentachloroethane	169	48	(Eight peak index of mass spectra)
			167	37	100		167	100	
			166	13	35		166	60	
			165	27	73		165	78	
			164	8	22		164	46	
			119	39	106		119	97	
			117	37	100		117	99	
			82	3	9		82	61	
8	6	19.7							
9	7	20.2							

APPENDIX E

H. SPECTRAL DATA

(1) Infrared:

Literature Values

Instrument: Beckman IR-12

Cell: 0.015 mm liquid cell, sodium chloride windows

Results: (See Figure 5)

Consistent with literature spectrum. (Sadtler Research Laboratories)

(2) Ultraviolet/Visible:

Instrument: Cary 118

Results: No absorbance detected between 350 and 800 nm (visible range). No maxima between 213 and 350 nm (ultraviolet range) but a gradual increase in absorbance toward the cutoff at 213 nm

No literature reference found.

Concentration: 1% v/v

Solvent: Methanol

(3) Nuclear Magnetic Resonance:

Instrument: Varian HA-100

Solvent: Neat, tetramethylsilane added

Determined	Literature Value
Assignments: See Figure 6 (a)s, δ 6.15 ppm	δ 6.12 ppm (Jouvre, 1966)
Integration ratios: (a) 1.00	

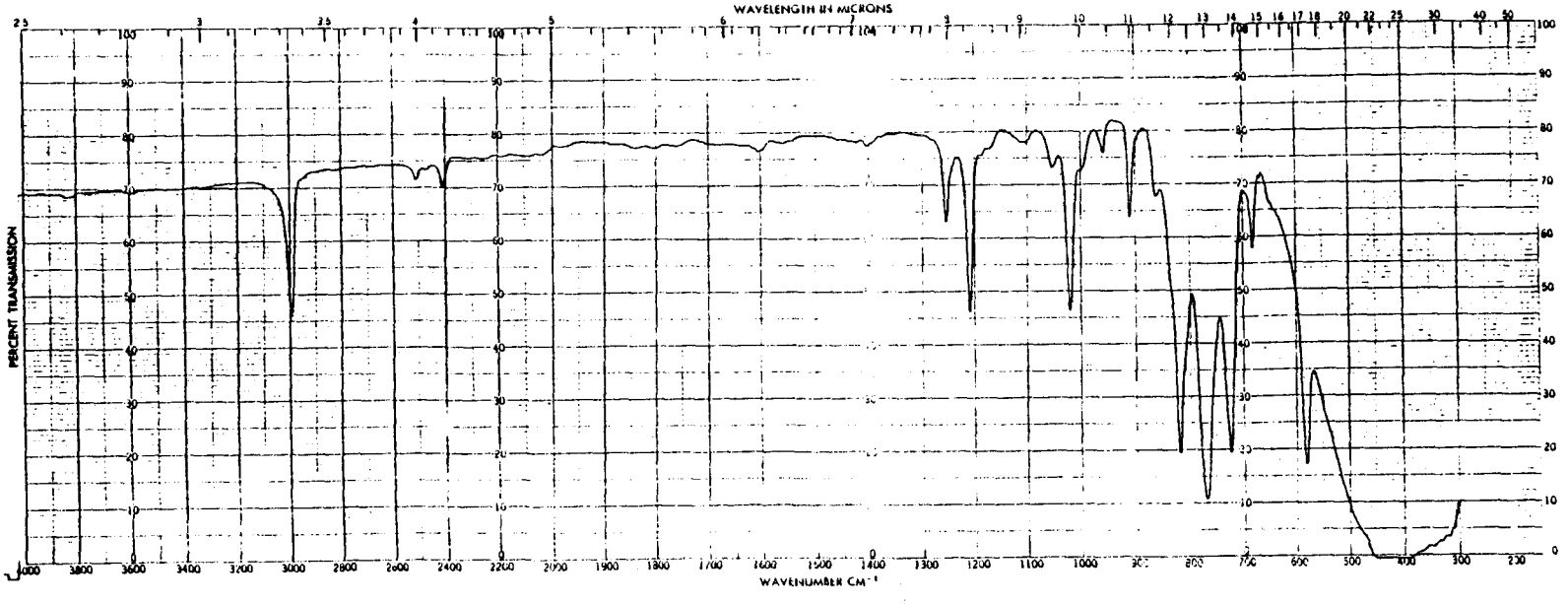

Figure 5. Infrared Absorption Spectrum of Pentachloroethane (Lot No. C041676)

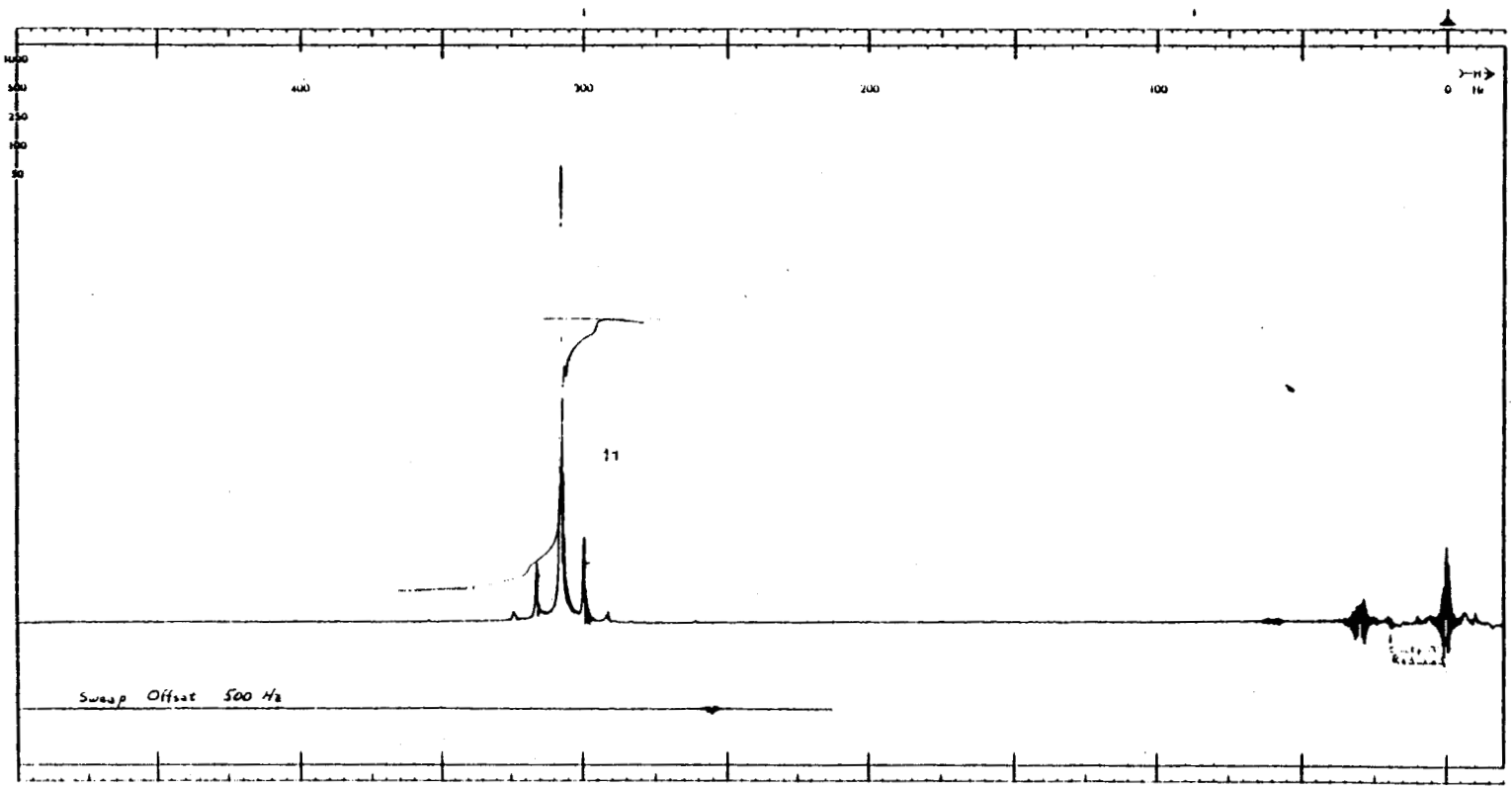

Figure 6. Nuclear Magnetic Resonance Spectrum of Pentachloroethane (Lot No. C041676)

APPENDIX F

ANALYSIS OF PENTACHLOROETHANE
(LOT NO. CO102077)
MIDWEST RESEARCH INSTITUTE
(TWO-YEAR STUDY)

APPENDIX F

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	11.87	0.50	87.63
Determined	12.02	0.54	87.33
	12.14	0.44	87.16

B. WATER ANALYSIS

(Karl Fisher) 0.013% ±0.001 (δ)%

C. VAPOR-PHASE CHROMATOGRAPHY

(1) Detection of impurities

Instrument: Tracor MT 220
Detection: Flame ionization
Carrier gas: Nitrogen

(a) System 1

Inlet temperature: 150°C

Detector temperature: 205°C

Carrier flow rate: 70 cc/min.

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass

Oven temperature program: 5 min. at 50°C, then 50 to 170°C at 10°C/min.

Sample injected: 4 μl neat liquid, diluted to 1.0% and 0.5% in pentane to quantitate the major peak and check for overloading.

RESULTS: Major peak and 13 impurities (Table F1). One impurity had an area 2.1% of the major peak. The other 12 impurities had a total area 2.4% of the area of the major peak. Peak 9, which quantitated as 2.1%, was identified by vapor-phase chromatography and vapor-phase chromatography/mass spectrometry as hexachloroethane. Hexachloroethane was quantitated against a 2% standard in Section C-2-e.

(b) System 2

Inlet temparature: 200°C

Detector temperature: 230°C

Carrier flow rate: 70 cc/min.

Column: 10% Carbowax 20M-TPA, on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D., glass

Oven temperature program: 5 min. at 50°C, then 50 to 200°C at 10°C/min.

Sample injected: 5 μl neat liquid, diluted to 1.0% and 0.5% in hexanes to quantitate the major peak and check for overloading.

RESULTS: Major peak and 14 impurities (Table F2). The areas of the 14 impurities total 2.0% of the area of the major peak.

TABLE F1. VAPOR-PHASE CHROMATOGRAPHY DATA: SYSTEM 1

Peak	Retention Time (min.)	Retention Time (Relative to Pentachloroethane)	Area (Percent of Pentachloroethane)
1	1.2	0.10	0.07
2	5.3	0.41	0.15
3	9.7	0.76	0.84
4	11.2	0.88	0.04
5	11.7	0.92	0.07 shoulder
6	11.9	0.93	0.54
7	12.1	0.95	0.28
8	12.8	1.00	100
9	14.1	1.10	2.10
10	15.0	1.18	0.01
11	15.8	1.24	0.19
12	16.3	1.28	0.15
13	17.1	1.34	0.04
14	22.4	1.76	0.01

TABLE F2. VAPOR-PHASE CHROMATOGRAPHY DATA: SYSTEM 2

Peak	Retention Time (min.)	Retention Time (Relative to Pentachloroethane)	Area (Percent of Pentachloroethane)
1	1.3	0.09	0.09
2	3.7	0.26	0.19
3	4.6	0.33	0.82
4	10.7	0.76	0.01
5	10.9	0.78	0.01
6	13.2	0.94	0.56
7	14.0	1.00	100
8	14.5	1.04	0.02
9	15.7	1.12	0.01
10	16.2	1.16	0.01
11	16.3	1.17	0.01
12	16.8	1.20	0.06
13	17.2	1.24	0.09
14	17.9	1.28	0.05
15	18.3	1.31	0.05

(2) Identification and quantitation of impurities

Instrument: Tracor MT-220

Detector: Flame ionization

Carrier gas: Nitrogen

Carrier flow rate: 70 cc/min.

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass

(a) System 1 (Acetone)

Inlet temperature: 205°C

Detector temperature: 225°C

Oven temperature program: 50°C, isothermal

Standards (4 μl) of 0.1% acetone in o-dichlorobenzene were injected. Acetone had a retention time of 1.3 minutes. Pentachloroethane had a peak with a retention time of 1.3 mnutes when injected neat under the same conditions which was enhanced by the addition of acetone. The acetone in the sample was quantitated against the 0.1% standard in o-dichlorobenzene.

CONCLUSIONS: The sample was found to contain acetone at a concentration of 0.082 $\pm$0.007 (δ)%.

(b) System 2 (Trichloroethylene)

Inlet temperature: 155°C

Detector temperature: 205°C

Oven temperature program: 50°C isothermal

Standards (4 μl) of 0.15% trichloroethylene in o-dichlorobenzene were injected. Trichloroethylene had a retention time of 5.4 minutes. Neat pentachloroethane had a peak with a retention time of 5.4 minutes when injected under the same conditions, which was enhanced by the addition of trichloroethylene. Trichloroethylene in the sample was quantitated against the 0.15% standard in o-dichlorobenzene.

CONCLUSION: The sample contained 0.125 $\pm$0.001 (δ)% trichloroethylene

(c) System 3 (Tetrachloroethylene)

Inlet temperature: 155°C

Detector temperature: 215°C

Oven temperature program: 75°C isothermal

Standards (4 μl) of 0.3% tetrachloroethylene in pentane were injected. Tetrachloroethylene had a retention time of 6.2 minutes. Pentachloroethane had a peak with a retention time of 6.2 minutes when injected under the same conditions at a concentration of 10% in pentane. This peak was enhanced by the addition of tetrachloroethylene. The tetrachloroethylene in the 10% pentachloroethane in pentane was quantitated against the 0.3% standard of tetrachloroethylene in pentane.

CONCLUSIONS: The sample contained 0.047 $\pm$0.001 (δ)% tetrachloroethylene.

(d) System 4 (1,1,2,2-Tetrachloroethane)

Inlet temperature: 215°C

Detector temperature: 255°C

Oven temperature program: 100°C isothermal

Standards (5 μl) were injected containing 0.1% 1,1,2,2-tetrachloroethane in hexanes. 1,1,2,2-Tetrachloroethane had a retention time of 5.2 minutes. Pentachloroethane had a peak with a retention time of 5.2 minutes when injected neat under the same conditions, which was enhanced by the addition of 1,1,2,2-tetrachloroethane. 1,1,2,2-Tetrachloroethane in the sample was quantitated against the 0.1% standard in hexanes.

CONCLUSIONS: The sample was found to contain 0.0280 ±0.0002 (δ)% 1,1,2,2-tetrachloroethane.

(e) System 5 (Hexachloroethane)

Inlet temperature: 155°C

Detector temperature: 220°C

Oven temperature program: 120°C isothermal

Standards (5 μl) were injected containing 2% hexachloroethane in hexanes. Hexachloroethane had a retention time of 6.7 minutes. Pentachloroethane had a peak with a retention time of 6.2 minutes when injected neat under the same conditions, which was enhanced by the addition of hexachloroethane. The hexachloroethane in the sample was quantitated against the 2% standard in hexanes.

CONCLUSIONS: The sample contained 4.23 ± 0.06 (δ)% hexachloroethane.

D. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

Instrument: Varian MAT CH4B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT 2000 MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 x 4 mm I.D.

Inlet temperature: 170°C

Oven temperature program: 5 min. at 50°C, then 50°-170°C at 10°C/min.

Sample injected: 1 μl neat liquid

Carrier gas: Helium

Carrier gas flow rate: 30 ml/min.

RESULTS: Major peak and 10 impurities (Tables F3 and F4). Two of these were caused by system decomposition. Eight were identified as impurities present in the sample.

TABLE F3. VAPOR-PHASE CHROMATOGRAPHY DATA

Peak	Retention Time (min.)	Retention Time (Relative to Pentachloroethane)	Corresponding Peak in Table F1
1	3.7	0.17	1
2	14.3	0.66	2
3	15.4	0.71	Not observed (<0.01%)
4	18.2	0.84	3
5	19.9	0.92	4
6	20.5	0.94	6
7	20.8	0.96	7
8	21.7	1.00	8
9	25.0	1.15	9
10	28.3	1.30	10 (tentative)
11	38.3	1.76	11 (tentative)

TABLE F4. MASS SPECTROMETRY DATA

Peak (Same as Table F3)	Mass	Percent of Base Peak	Assignment	Literature		
				Mass	Percent of Base Peak	Reference
1	43	100	Acetone	43	100	(Eight peak index
	58	46		58	33	of mass spectra)
	15	22		15	27	
	42	7		42	11	
	27	4		27	5	
	39	3		39	4	
	29	21		29	4	
	26	4		26	3	
2	130	100	Trichloroethylene	130	98	(Eight peak index
	132	96		132	94	of mass spectra)
	95	83		95	100	
	97	55		97	64	
	134	31		134	30	
	60	19		60	31	
	99	8		99	11	
	62	8		62	10	
3	43	100	1,1,1-Trichloropropane	43	100	(Eight peak index
	15	10		15	12	of mass spectra)
	83	3		83	6	
	27	3		27	5	
	125	Not observed		125	4	
	63	4		63	4	
	47	Not observed		47	4	
	85	Not observed		85	3	
4	166	100	Tetrachloroethylene	166	100	(Eight peak index
	164	99		164	78	of mass spectra)
	129	88		129	64	
	131	87		131	62	
	168	83		168	48	
	133	25		133	20	
	94	24		94	21	
	96	15		96	14	
5	83	100	1,1,2,2-Tetrachloroethane	83	100	(Eight peak index
	85	62		85	63	of mass spectra)
	131	15		131	8	
	168	13		168	8	
	95	12		95	11	
	87	9		87	10	
	61	9		61	8	
	60	6		60	8	

TABLE F4. MASS SPECTROMETRY DATA (Continued)

Peak (Same as Table F3)	Mass	Percent of Base Peak	Assignment	Literature		
				Mass	Percent of Base Peak	Reference
6	132	100	Trichloroethylene	132	94	(Eight peak index
	130	98	from system decomposition	130	98	of mass spectra)
	95	93		95	100	
	97	55		97	64	
	134	30		134	30	
	60	25		60	31	
	99	10		99	11	
	62	10		62	10	
7	166	100	Tetrachloroethylene	166	100	(Eight peak index
	164	82	from system decomposition	164	78	of mass spectra)
	131	64		131	62	
	129	64		129	64	
	168	46		168	48	
	94	27		94	21	
	96	21		96	14	
	133	20		133	20	
8	117	100	Pentachloroethane	117	99	(Eight peak index
	119	98		119	97	of mass spectra)
	167	92		167	100	
	165	68		165	78	
	169	44		169	48	
	166	12		166	60	
	164	6		164	46	
	82	4		82	61	
9	117	100	Hexachloroethane	117	100	(Eight peak index
	201	97		201	81	of mass spectra)
	119	92		119	87	
	166	78		166	42	
	203	60		203	51	
	199	59		199	49	
	164	57		164	42	
	121	28		121	31	
10	191	100	Pentachlorobutadiene	191	100	(Eight peak index
	189	69		189	78	of mass spectra)
	226	58		226	46	
	193	46		193	48	
	119	31		119	29	
	156	25		156	30	
	154	20		154	31	
	84	17		84	44	
11	155	100	1,2,4,4-Tetrachlorobutadiene	155	100	(Eight peak index
	157	91		157	96	of mass spectra)
	192	54		192	52	
	190	43		190	38	
	119	40		119	46	
	159	30		159	30	
	194	28		194	24	
	121	28		121	30	

APPENDIX F

With flame ionization detection, Section C-1-a, a cluster of two peaks and a shoulder, numbered Peaks 5, 6, and 7, were observed eluting shortly before the major peak. In the mass spectrum, two components were identified in this region, trichloroethylene and tetrachloroethylene which were formed by system decomposition. It is believed that Peak 5 by flame ionization detection is not a separate component but a shoulder formed during decomposition.

The assignment of peaks 10 and 11 in the mass spectrum as pentachlorobutadiene and 1,2,4,4-tetrachlorobutadiene must be considered tentative for several reasons. Two peaks, 11 and 12, in Section C-1-a were observed by flame ionization detection in the region of Peak 11, but only one peak was observed in the mass spectrum. Peak 10 is assigned as pentachlorobutadiene and Peak 11 as 1,2,4,4-tetrachlorobutadiene, but it is probable that tetrachlorobutadiene would have a shorter retention time than pentachlorobutadiene. No standards were commercially available to spike the sample and determine which peak is enhanced. However, the match with the literature spectra is good, and it appears that compounds with these or very similar structures are present as impurities.

Specific ion searches were run for masses 47 and 83 characteristic of chloroform, and masses 119 and 131 characteristic of 1,1,1,2-tetrachloroethane. Masses 47 and 83 were both observed under Peaks 2, 4, 8, 9 and 11, and masses 119 and 131 were both observed under Peaks 4, 8 and 9, but the ratios of these masses were wrong for these peaks to be chloroform and 1,1,1,2-tetrachloroethane, and these peaks were identified as other compounds.

CONCLUSIONS: The sample does not contain $>0.01\%$ chloroform or 1,1,1,2-teterachloroethane. The sample contains acetone, trichloroethylene, hexachloroethane as well as pentachloroethane, the major component. It also contains tetrachlorobutadiene and pentachlorobutadiene or compounds of similar structure.

E. SPECTRAL DATA

(1) Infrared:

Instrument: Beckman IR-12

Cell: Thin film between AgCl plates

RESULTS: (See Figure 7)

Literature Values

Consistent with literature spectrum. (Sadtler standard spectra)

(2) Ultraviolet/Visible:

Instrument: Cary 118

No absorbance between 350 and 800 nm (visible region). No maximum between 212 and 350 nm (ultraviolet region) but a gradual increase in absorbance toward the solvent cutoff at 212 nm.

Concentration: 1%, 0.1%, and 0.01%

Solvent: Methanol

No literature reference found.

(3) Nuclear Magnetic Resonance:

Instrument: Varian EM-360 60 MHz

Solvent: Neat, tetramethylsilane added

Assignments: (See Figure 8)

(a) S, δ 6.11 ppm

(b) δ 2.14 ppm

Integration Ratios:

(a) 1.00

(b) <0.01

Consistent with literature spectrum. (Sadtler standard spectra)

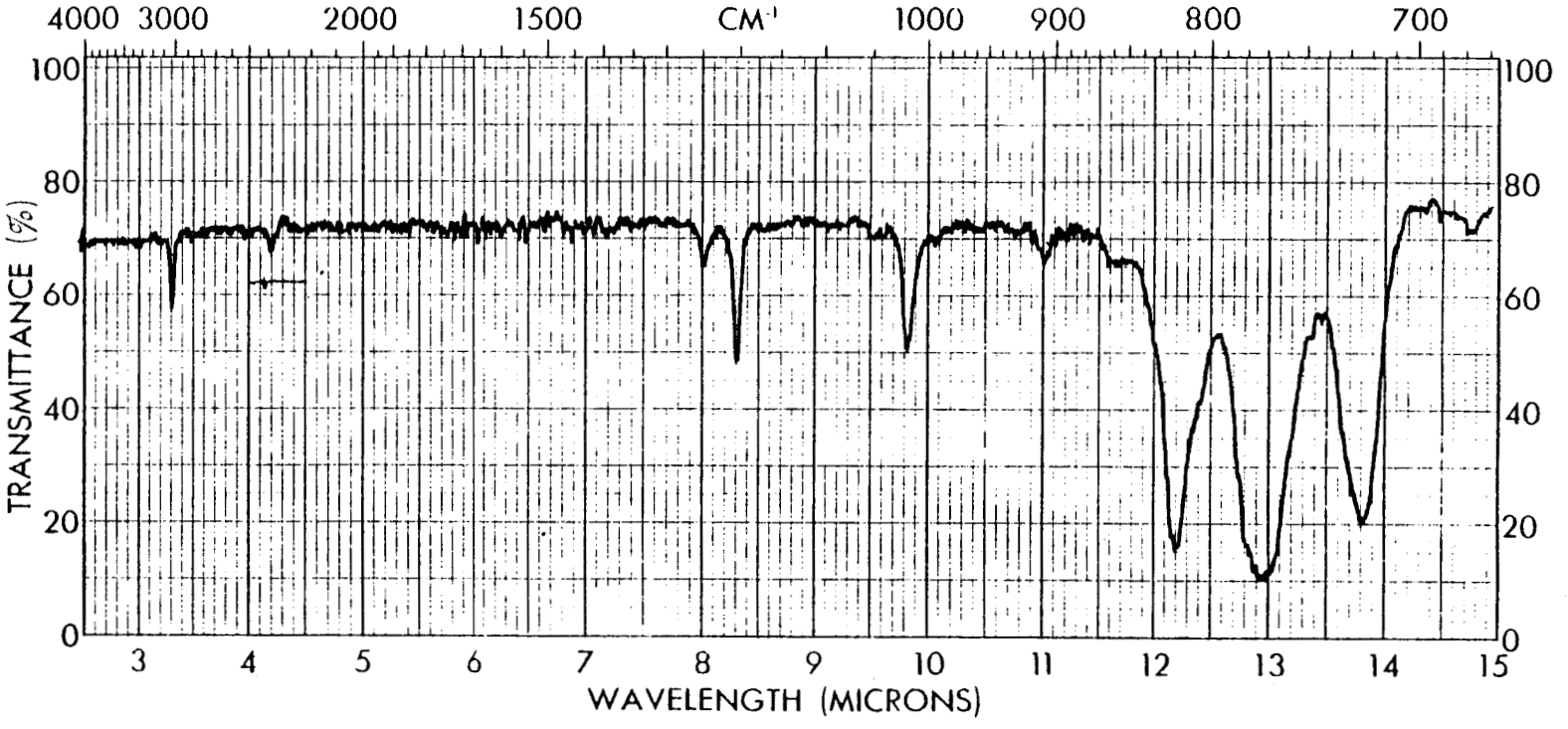

Figure 7. Infrared Absorption Spectrum of Pentachloroethane (Lot No. C0102077)

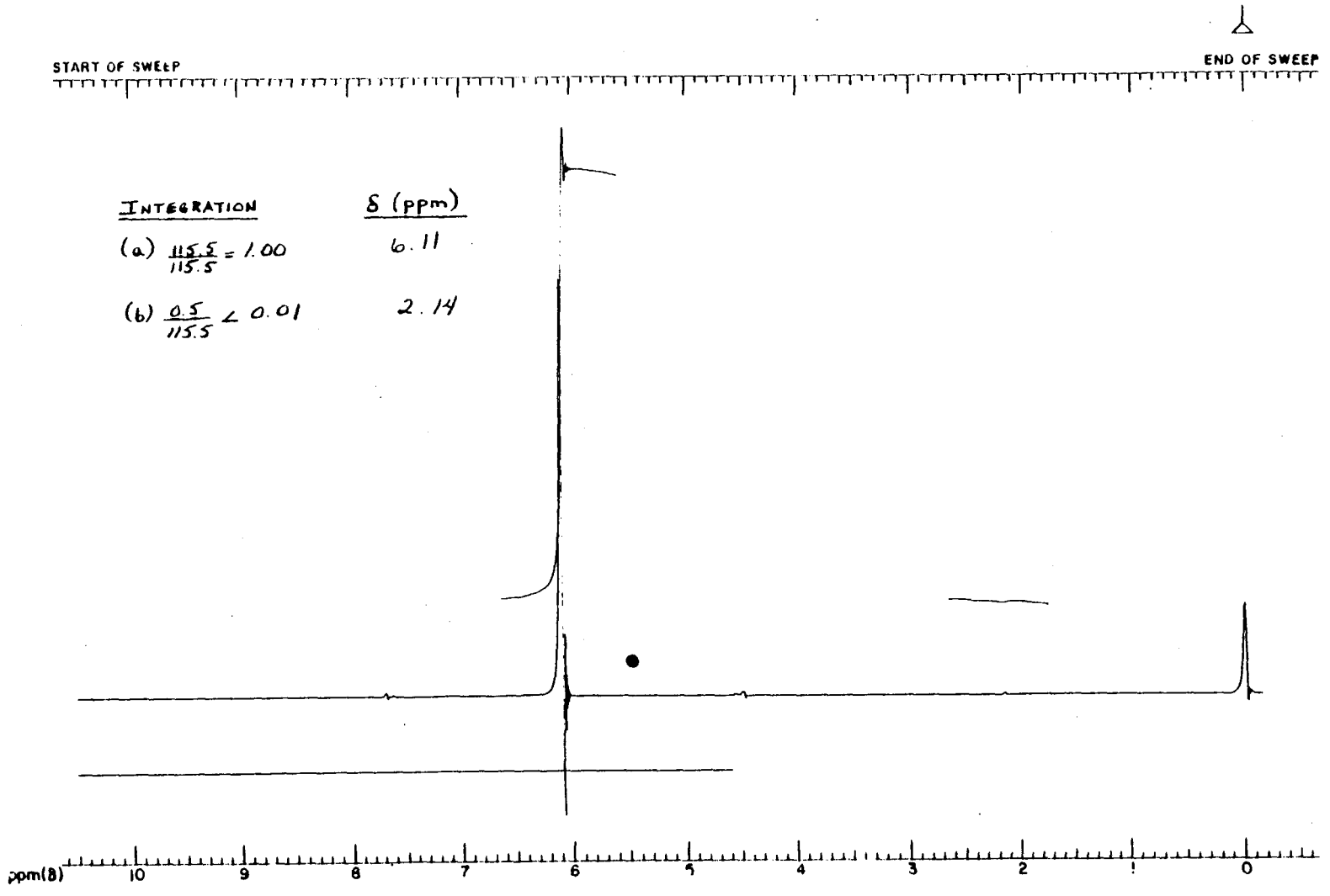

Figure 8. Nuclear Magnetic Resonance Spectrum of Pentachloroethane (Lot No. CO102077)

APPENDIX G

ANALYSIS OF PENTACHLOROETHANE FOR STABILITY IN CORN OIL MIDWEST RESEARCH INSTITUTE

APPENDIX G

A. SAMPLE PREPARATION

A 1% (w/v) sample solution of pentachloroethane in corn oil was prepared for each day of the study as follows: 10 ml of corn oil was transferred into a 50-ml septum vial, the vial was sealed, and then approximately 95 mg of pentachloroethane was added via a 100-μl syringe. The samples were shaken and stored at room temperature from 1 to 7 days, respectively.

B. EXTRACTION AND ANALYSIS

The samples were extracted with 20 ml of methanol, which was injected into the sample vial via a 10-ml syringe. Samples for analysis were taken directly from the top (methanol) layer and analyzed by vapor-phase chromatography using the following system.

Instrument: Bendix 2500

Column: 10% Carbowax 20 M on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D., glass

Detection: Flame ionization

Oven temperature: 130°C, isothermal

Inlet temperature: 250°C

Detector temperature: 280°C

Retention time of test compound: 3.00 minutes.

C. RESULTS

End of Day	Average % Compound *(a)*
1	0.98 ± 0.05
2	0.97 ± 0.05
3	0.97 ± 0.05
4	1.01 ± 0.05
5	1.02 ± 0.05
6	1.00 ± 0.05
7	1.03 ± 0.05

(a) Corrected for a spiked recovery value of 60.2%.

D. CONCLUSION

Pentachloroethane mixed in corn oil is stable for 7 days at room temperature.

APPENDIX H

ANALYSIS OF PENTACHLOROETHANE IN CORN OIL FOR CONCENTRATIONS OF PENTACHLOROETHANE GULF SOUTH RESEARCH INSTITUTE

The sample (1.0 ml) was diluted with isooctane (10 ml) and an aliquot was analyzed by gas chromatography.

Instrument Parameters

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport

Temp: 120°C

Flow: ~ 30 ml/minute

Detector: Flame Ionization Detector

Temp: 250°C

RESULTS: See Table H1.

TABLE H1. ANALYSIS OF PENTACHLOROETHANE IN CORN OIL

Date Mixed	Date Used Week of:	Concentration of Pentachloroethane *(a)* in Samples with Target Concentrations of: 30 mg/ml	50 mg/ml
1/4/78	1/5/78	—	49.1
3/29/78	3/30/78	—	50.2
5/4/78	5/5/78	—	47.0
8/3/78	8/4/78	—	50.6
9/22/78	9/23/78	—	50.6
9/29/78	9/30/78	—	54.5
1/4/79	1/5/79	—	49.0
3/20/79	3/21/79	—	47.1
5/31/79	6/1/79	—	53.9
7/26/79	7/27/79	28.0	—
10/11/79	10/12/79	31.9	—
11/2/79	11/3/79	32.6	—
12/6/79	12/7/79	30.2	—
Mean (mg/ml)		30.7	50.2
Standard Deviation		2.05	2.62
Coefficient of Variation (%)		6.7	5.2
Range (mg/ml)		28.0-32.6	47.0-54.5
Number of Samples		4	9

(a) Data presented are the averages of the results of duplicate analyses.

APPENDIX I

MEAN BODY WEIGHTS OF ANIMALS ADMINISTERED PENTACHLOROETHANE BY GAVAGE IN THE TWO-YEAR STUDY

TABLE I1. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF RATS ADMINISTERED PENTACHLOROETHANE BY GAVAGE IN THE TWO-YEAR STUDY

		Mean Body Weight (grams)			Body Weight Relative to Controls *(a)* (percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
MALE	0	133	140	138	+ 5	+ 4
	2	181	185	181	+ 2	0
	22	354	351	353	− 1	0
	42	395	394	381	0	− 4
	62	427	420	420	− 2	− 2
	82	447	429	432	− 4	− 3
	102	428	403	395	− 6	− 7
	103	420	405	400	− 4	− 5
FEMALE	0	101	100	102	− 1	+ 1
	2	129	126	125	− 2	− 3
	22	193	183	189	− 5	− 2
	42	213	203	201	− 5	− 6
	62	241	222	218	− 8	−10
	82	271	251	243	− 7	−10
	102	277	247	242	−11	−13
	103	276	255	242	− 8	−12

(a) Weight relative to controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

TABLE I2. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF MICE ADMINISTERED PENTACHLOROETHANE BY GAVAGE IN THE TWO-YEAR STUDY

		Mean Body Weight (grams)			Body Weight Relative to Controls *(a)* (percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
MALE	0	27	27	26	0	− 4
	2	29	31	30	+ 7	+ 3
	22	42	44	37	+ 5	−12
	42	49	49	—	0	—
	62	51	46	—	−10	—
	82	49	42	—	−14	—
	102	44	36	—	−18	—
	103	44	36		−18	
FEMALE	0	20	20	20	0	0
	2	22	23	24	+ 5	+ 9
	22	28	30	29	+ 7	+ 4
	42	37	36	30	− 3	−19
	62	38	37	30	− 3	−21
	82	42	34	—	−19	—
	102	41	27	—	−34	—
	103	39	34	—	−13	—

(a) Weight relative to controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

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